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DIAGNOSIS AND TREATMENT OF LARYNGEAL TUMORS

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This paper will be devoted to the symptoms, diagnosis and treatment of the more common types of lesions of the larynx.

The symptoms of any lesion of the larynx vary, depending on the size and location of the lesion. Should it occur on one or both vocal cords, as is common in 80 per cent of the cases, hoarseness is the first and often the only symptom present. On the other hand, should the epiglottis, aryepiglottic fold, pyriform sinus, ventricular band or any site distant to the vocal cords be affected, hoarseness may not be evident. Dyspnea, cough and croupy tendencies are other symptoms that may be noted. Pain is rarely experienced.

EXAMINATION OF THE PATIENT

The diagnosis of these lesions is the most important issue in this discussion. There is nothing difficult in making a diagnosis if a definite routine has been established and is carefully followed in every case. First, it must be remembered that more is seen with the laryngeal mirror than with any type of laryngoscope. Mirror examination offers a complete view of the entire larynx, which in turn permits examination of the color of the cords and laryngeal mucous membrane and, most noteworthy of all, inspection of the mobility of the cords on inspiration and phonation. The entire larynx, as well as the anterior commissure, must be accurately visualized. It is difficult to see the anterior commissure in many patients, particularly in those patients with a low-hanging epiglottis, a short, thick neck, a large tongue and pronounced gag reflexes. It must be borne in mind that many malignant growths start in this area, and, regardless of the amount of time consumed, this portion of the larynx must be clearly seen before the examination can be called complete.

Paramount in importance is the position of the patient. He must be placed in a good light and instructed to sit with shoulders slightly thrown forward and head flung back. A short discourse before examination concerning the art of relaxation can prove beneficial to all concerned. It should be emphasized that he keep his eyes open, look directly at the physician and breathe regularly through his mouth, this last being his only concern at this particular time. The number of children in whom indirect laryngoscopy can be used, once their confidence has been obtained, is surprising. If necessary, the larynx must be cocainized, thus enabling the physician to view every vestige of it and assuring him of complete visualization. Many children require a direct laryngoscopic examination with general anesthesia before a diagnosis can be made.

On completion of the examination, should a tumor be discovered, the next procedure is removal of that tumor by direct laryngoscopy. A roentgenogram of the chest and Wassermann test of the blood are routinely done in all cases, and if malignancy of the larynx is suspected, tomographs and lateral roentgenograms of the neck are taken. After removal of the tumor, it should be sent to the laboratory for pathologic examination. No matter how many times or how often these tumors are encountered, the specimens should be sent to the laboratory for examination, for occasionally an incorrect diagnosis may be made.

Twenty-seven years ago, Dr. MacKenty stated, "Judging from the advanced condition of the great majority when they come for operation, the diagnosis of carcinoma of the larynx must either be extremely difficult or poorly understood by the profession. In hundreds of cases seen by me, a pathetically small number can be assured of a hopeful outcome. In many instances the fault lies with the patient not seeking an opinion earlier, but in far too many, they have been under observation and treatment for months."

This statement seems to be as true today as it was twenty-seven years ago. In this enlightened age of laryngology, this should not be, for, if in all laryngeal examinations one follows an established and nonflexible routine, I am certain that one will detect many early laryngeal carcinomas that can be cured by operation or roentgen therapy. I have observed many patients with laryngeal malignancy which had been erroneously treated for a long period whose hoarseness had been ascribed to chronic laryngitis or chronic sinusitis, with postnasal drip named as the causative factor. Other patients have had tonsillectomy prescribed as a cure-all. Recently a patient was advised to live in Arizona for a few months, since his doctor felt that a change of climate would cure his laryngitis. While he was en route, an emergency tracheotomy had to be done, since his airway was almost completely occluded by a large laryngeal carcinoma. Unfortunately, hope is denied these patients, and proper treatment is of no avail. All these errors could be avoided if, when a noticeable change in voice or a persistent hoarseness continues for a period of three weeks, the larynx is completely examined and proper treatment instituted.

If a physician is not satisfied with his visualization of the larynx, he should consult other laryngoscopists, and, if there is any further doubt, a cytologic, sponge or tissue examination should be done. Cancer of the larynx, no less than cancer elsewhere, must be diag-

From the Manhattan Eye, Ear and Throat Hospital.
Read before the Section on Laryngology, Otology and Rhinology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1949.

nosed early in order to prolong or save the patient's life. To wait or to procrastinate is to gamble with the patient's chances of relief or cure. The patient's welfare should have first consideration by any conscientious physician.

The diagnosis of these tumors cannot be too greatly stressed in this discussion. Thousands of lives will be saved if the physician can make an accurate diagnosis early, whether he performs the operation himself or refers the patient to one more familiar with this type of operation or to the roentgen therapist. Irrespective of the type of tumor involved, a careful mirror examination must be done, and often repeated reexaminations and possibly direct laryngoscopy are required. The majority of these tumors may be removed with direct or suspension laryngoscopy, while others necessitate a thyrotomy or lateral pharyngotomy. Regardless of the method employed, a biopsy should be made to ascertain the type of tumor present. Biopsy and pathologic examination must be done in all cases of tumor of the larynx.

Tumors Seen in the Laryngeal Clinic of the Manhattan Eye, Ear and Throat Hospital (1944-1949)

Epidermoid Carcinoma		**Papilloma**	
Grade I	60	Simple	136
Grade II	216	Multiple	20
Grade III	86	Hyperkeratotic	82
Grade IV	13	Hyperkeratotic with malignant changes	38
Ungraded	14		
Total	389	Total	276
		Cysts	12
		Contact ulcer	12
		Fibroma	5
Polyp		Fibroangioma	3
Simple	549	Fibroleiomyoma	1
Fibrous	14	Chordoma	1
Cystic	13	Rhabdomyosarcoma	1
Papillomatous	3	Lymphoma	2
Hemorrhagic	14	Paraffinoma	1
Hyaline	8	Sarcoma	1
Ulcerated	4	Scleroma	2
Lymphangiomatous	1	Vocal nodules	21
		Lipoma	1
Total	606	Mixed tumor	1

POLYP

The most common tumors seen in the clinic at the Manhattan Eye, Ear and Throat Hospital are polyps, papillomas, carcinomas, vocal nodules and contact ulcers. Strictly speaking, a polyp is not a tumor but edema of the connective tissues, filled with varicosities. However, as the polyp is the most common cause of hoarseness and is so often confused with papilloma and carcinoma, I think it in order to say a few words regarding it.

Polyps may be single or multiple, sessile or pedunculated, or there may be polypoid degeneration of the whole cord. They usually occur as a single glistening mass attached to the cord by a thin pedicle. Treatment consists of removal with direct laryngoscopy, with either the cup or subglottic forceps. When either cord is polypoid throughout, stripping is the operation of choice. The tendency of recurrence is rare.

PAPILLOMA

Papilloma is a warty growth. There is a distinct difference, histologically and clinically, between papilloma and polyp, and yet, frequently enough, care is not taken to differentiate between these two. Histologically, a polyp is edema of the connective tissue beneath the epithelium which causes a bulging. As a result of the pressure caused by the polyp, the epithelium becomes thin and nonpapillated. The polyp is usually associated with thrombosis and varicosities of the veins and is analogous to a hemorrhoid. A papilloma is a papillary hyperplasia of the surface epithelium, with the basement membrane remaining intact. It is analogous to a cauliflower growth. Papillomas are usually divided into papillomas of childhood, simple papillomas and hyperkeratotic papillomas.

In childhood this condition is most frequently seen as multiple papillomas, while in adult life the single papilloma is more common. Usually there is a history of increased hoarseness and, at times, difficulty in breathing. Many things, such as enlarged tonsils and thymus, must be considered as possible contributing causes. With children a mirror examination is usually impossible; however, direct laryngoscopy will reveal a multiplicity of papillomas springing from the true and false cords. Papilloma of the larynx in childhood is usually self limited and ultimately heals spontaneously. Previously the treatment consisted of a semipermanent tracheotomy, with removal of the tube when laryngeal breathing was reestablished, (usually upward of five years). With modern technics and use of the laryngoscope, the logical treatment is repeated removal of the papillomas as they recur. However, particular care must be taken not to damage the important and permanent structure of the larynx. Often papillomas recur at frequent intervals until the age of puberty, when they finally disappear. Occasionally, even in childhood, a single removal of the papillomas will effect a permanent cure. Tracheotomy for this condition must, if possible, be avoided.

Fortunately, these multiple papillomas of childhood, which try the patience and skill of the physician, are fast disappearing and are rarely seen in the clinic today. This is one condition wherein the antibiotics cannot be given credit, since the decline was definitely noticeable before the advent of these drugs. I feel that the reason for this decline is the modern understanding of diet during infancy and childhood, the use of vitamins, periodic school health examinations, improved general sanitation and removal of tonsils and adenoids.

In the adult the papilloma is usually single, although it may be multiple. The treatment is the same in adults as in children, removal with direct laryngoscopy. Occasionally these papillomas invade the underlying structure (submucosa) and change characteristics, which eventually results in their assuming a true malignant form. This is especially true of recurrent multiple papillomas. In these cases it is wise to have the patients return at frequent intervals for reexamination.

HYPERKERATOTIC PAPILLOMA

This type of lesion may be situated anywhere in the larynx, pyriform fossa, base of the epiglottis or on the false and true cords, but it is more commonly found in the middle or anterior portion of the true cords and is always to be considered a precancerous lesion. Nowhere else in the body is the hyperkeratotic papilloma more significant. Probably the tongue or the cervix of the uterus follows next in importance as far as the location of a precancerous papilloma is concerned. The true vocal cords by far exceed the other structures in significance and prognostic importance so far as early examination and interpretation of this lesion are concerned. Recurrent multiple papillomas or hyperkeratotic papillomas must always be looked on as premalignant, and patients with these lesions must be closely watched for years.

VOCAL NODULES

Vocal nodules, or singers' nodes, are almost always bilateral. They appear as small nodules on the edge of the cords at the junction of the anterior and middle thirds and are made up of fibrous or loose vascular inflammatory tissue. They are always benign. They are supposedly caused by singing or speaking in the wrong vocal register. Many persons, such as orators, clergymen and school teachers, who use their voices a great deal may be bothered with these nodules.

Treatment.—Many feel that vocal rest is sufficient to effect the disappearance of these nodules, but I believe they should be carefully removed with direct laryngoscopy. Special care must be taken not to injure the cord. The operation should be followed by complete vocal rest.

CYSTS

Cysts are almost always benign. They are usually attached to the anterior surface of the epiglottis but are occasionally seen on one cord.

Treatment.—Treatment consists of removal with direct laryngoscopy.

CONTACT ULCER

Contact ulcer is a chronic ulcer occurring on one or, more frequently, on both vocal cords at the vocal process.

Etiologic change.—Abuse of the voice, such as constant shouting and the excessive use of alcohol and tobacco, causes contact ulcers. With a cartilaginous process hammering against the one on the opposite side, a small area of necrosis starts under the tip of the vocal process involving the perichondrium.

Treatment.—Treatment consists of the careful removal of the superfluous granulomatous tissue. The patient must then observe absolute silence, sometimes for a year. Galvano cautery and applications of silver nitrate are almost useless.

CANCER OF THE LARYNX

Cancer of the larynx is the most important of all tumors of the larynx. In approximately 80 per cent of all cases, cancer of the larynx starts on the vocal cord, the first symptom being hoarseness. If patients with cancer of the larynx could be seen during this early stage and treated at this time, the percentage of cures would be close to 100 per cent. In this stage these patients should undergo laryngofissure, which offers cures in 80 per cent of the cases. As Dr. MacKenty said years ago, "All lesions of the larynx should be looked on with suspicion until they are proved not to be malignant."

The treatment of cancer of the larynx depends on many things, size and location of the growth, mobility of the cord, age, general health and mental attitude of the patient and whether or not the glands of the neck are involved. All these factors should be considered at length before the physician decides what type of treatment is best suited for the individual patient. In an early cordal tumor, in which the lesion does not cross the anterior commissure or extend beyond the vocal process posteriorly and in which the cord moves freely, laryngofissure is the operation of choice. Cures can be obtained in about 80 per cent of cases involving this type of tumor, leaving a good, if somewhat husky, voice.

When the growth is seen early and is very small, involving one cord which is freely movable, one may remove it by simply biting it out with a cup forceps through the laryngoscope and fulgurating the base with the electric current, as brought out by LeJeune and New. Of course, these patients should be seen at frequent intervals after the removal of the growth.

When the growth involves the tip of the epiglottis, provided it has not invaded the posterior third, the epiglottis may be removed without disturbing the rest of the larynx. This may be done by means of an anterior incision through the neck or by suspension laryngoscopy.

On the other hand, when the growth has involved one cord and the anterior commissure, or has crossed over the anterior commissure, or when there is a binding down of the cord, or when the growth extends posteriorly or when the aryepiglottic fold is affected, laryngectomy is the operation of choice. The epiglottis should always be removed in laryngectomy, for in many cases, when the anterior commissure is reached, the base of the epiglottis may be invaded, which often escapes detection even on careful inspection with the mirror.

In the extrinsic cases with involvement of the glands of the neck, the larynx should be removed, followed by radical neck dissection. As soon as the neck is healed, an extensive course of roentgen therapy should be instituted.

In these extensive lesions, Arbuckle advocates the removal of the thyroid cartilage, followed by roentgen therapy, but I feel more secure in removing the entire larynx.

During the past ten years, I have learned to respect the roentgen therapist and his contribution to the field of laryngology. In our hospital there is close cooperation between the laryngeal clinic and the department of roentgen therapy, and I feel certain that both departments have benefited from this close association.

I believe that the end results of five year cures with roentgen therapy of early cordal cancer are on a par with those of laryngofissure. I stress the fact that these are cases of early cordal cancer, without impairment of mobility of the cord, subglottic extension, involvement of the arytenoid or crossing of the anterior commissure. If these signs are present, laryngectomy is the treatment of choice.

I believe that the roentgen therapist treating laryngeal cancer must specialize in this field (just as the surgeon must be trained and qualified in this branch of surgery) and must be able to examine a larynx with both head and laryngeal mirrors.

A female patient, age 22, had an early carcinoma, type II, involving the middle of her right cord. It seemed an ideal case for laryngofissure. I advised operation and she refused. She consulted a roentgen therapist and was given the usual course of therapy. She was alive and well at the time of this writing, ten years after she had been examined by me, with no recurrence of the growth. Another patient, an orderly at the hospital, had about the same type of lesion as did the aforementioned patient, an early carcinoma, type II, involving the middle of his right cord. He refused operation and had roentgen therapy. He was alive and free from carcinoma at the time of writing (nine years later). Another early carcinoma, type II, with an involvement of the middle third of the left cord, was seen in a man 40 years of age. He also refused operation and had roentgen therapy. He had had no recurrence of his growth to the time of writing (seven years later).

After seeing the results in these 3 cases, I thought possibly I could be wrong in thinking that surgical intervention was the only method of curing early cordal cancers, so I referred some of the clinic cases to the roentgen therapy department.

During the past six years my associates and I have referred 16 additional cases of early cordal cancer to the roentgen therapy department. Of the total of 19 patients, 18 are alive and well, with no recurrence to date.

Of the 18 patients with no recurrence, 1 patient had received treatment over 10 years previously; 1 patient over 9 years, 1 patient over 7 years, 1 patient over 6 years, 5 patients over 3 years, 4 patients over 2 years, 2 patients over 1 year and 3 patients under 1 year.

The patient who did not fare well was a man of 40 with a lesion involving the anterior third of the right cord. Four months after roentgen therapy the cord appeared to be practically normal. Five months later the patient returned to the clinic with severe chondritis involving the entire larynx, which necessitated tracheotomy. He remained in the hospital for several months and eventually underwent laryngectomy. His larynx was filled with carcinoma, type II. He was alive and well at the time of writing (two years later), with no recurrence.

The method of treatment today is the administration of divided doses of approximately 6,500 to 8,000 r for a period of thirty to forty days. The dose is given through small fields. Rarely does necrosis of cartilage or other tissue occur. In the past, when large fields and too intensive dosage were used, it was almost impossible to differentiate the tissues of the neck if a subsequent laryngectomy had to be performed. Today, with the divided doses and small fields, it is just as easy, if not easier, to remove the larynx after roentgen therapy.

I do not believe that roentgen therapy is a panacea for all laryngeal cancer, for it is known that subglottic growths, those involving the pyriform sinus and aryepiglottic folds and those with metastates to the lymph nodes respond poorly to roentgen therapy alone. Patients with these lesions should undergo laryngectomy and neck resection, followed by roentgen therapy. However, I believe that the cordal cancer suitable for laryngofissure should be treated by irradiation and closely watched. If there is a recurrence of the growth after therapy has been completed, a laryngofissure or laryngectomy may be done.

CONCLUSIONS

The most common symptom in tumors of the larynx is hoarseness, which may be trivial or serious. The otolaryngologist must determine which it is. If he examines the larynx carefully, following a strict routine in every case, he will make a correct diagnosis of practically every laryngeal lesion he sees. He must see every vestige of the larynx in every case before he calls his examination complete. A biopsy and pathologic examination must be done on all tumors of the larynx. The surgeon must determine in each case the course to be pursued, whether it be operation or roentgen therapy or both. The end results in five year cures with roentgen therapy of early cordal cancers are on a par with those of surgical intervention. Patients treated with roentgen rays can be watched every month; if there should be a recurrence, surgical procedures can be done at that time.

ABSTRACT OF DISCUSSION

Dr. Morley T. Smith, New Rochelle, N. Y.: Dr. Cunning has covered the subject well. I must take some exception to his enthusiasm for treatment of cancer of the larynx with roentgen rays. Many of these patients can and are being treated successfully with roentgen rays. If there is close cooperation between the department of roentgenology and the laryngologist, such as is found at the Manhattan Eye, Ear and Throat Hospital, where these cases are carefully followed, then roentgen treatment may be given a trial in early cases. In our experience in the cancer clinic of a general hospital many of these patients have gone to laryngologists, where the correct diagnosis has been made, and then have returned to the family doctor. Many general practitioners are inclined to encourage the patient to have roentgen treatment instead of operative treatment. In our clinic my associates and I often see the bad results, but I am sure there are many good results. After these patients finish their course of roentgen therapy, they are likely to assume that all is well; then, when they come back to us, the lesions are often inoperable. We have had thirty years or more of experience with laryngofissure, with a high percentage of cures. It is a simple operation; it can be done without much disturbance of function. One cannot escape the fact that satisfactory results have been obtained in a large number of the cases. Dr. Cunning states that the important aspect of his paper is diagnosis, in which I am particularly interested. He quoted MacKenty's statement of many years ago. Subsequently, Jackson was more definite, stating that more than 80 per cent of cancers of the larynx are curable. Yet the fact remains that 90 per cent of the persons with cancer of the larynx die from the disease. We have made little progress since that time. This certainly presents a challenge to the medical profession. Laryngologists do not need to be reminded of the importance of early diagnosis. If more stress were laid in the medical schools on the diagnosis, symptomatologic study and examination of the larynx, many lives that are now being lost would be saved. Dr. Cunning has stressed the simplicity of this examination. Over a number of years I have asked the interns who come to our tumor clinic what training they have had in the examination of the larynx. Although our interns come from the best schools, it has been surprising to find that they have not had any instruction in the examination of the larynx. This training should be followed up in their internship. Laryngologists should make a point of teaching these men how to examine the larynx properly.

Dr. Edward J. Whalen, Hartford, Conn.: Dr. Cunning reports fifteen varieties of benign tumor of the larynx. The Jacksons list twenty-one distinct types of benign tumor in this area. I have one more to add to this list, a tumor produced by a psoriasis lesion of the vocal cord. The suggestion has been made by Colonel Ash of the Army Medical Museum and accepted by many laryngologists, as well as pathologists, that some of these tumors may be grouped together because they have a common traumatic origin and because the varying growths and microscopic appearances are but successive stages in the same process. Hajek described a layer of loose connective tissue just below the epithelial surface. Reinke, continuing this study, gave a definitive description of this subepithelial layer, and Hajek, in a later report, gave the name Reinke's space to this layer beneath the surface eipthelium. This layer contains no lymph spaces or nodes. Its base is yellow elastic fiber overlying the muscle layer. These features are important. The sequence of events leading to the formation of these benign tumors can be followed clinically and histologically. Fibromas, nodes, nodules, polyps and varices all begin as a result of some form of vocal trauma. From this trauma there follows a protrusion and thickening of the connective tissue in Reinke's layer, resulting first in a fibroma, second in the exudation of serum into this loose tissue to form a polyp, third in the formation of new blood vessels, which appear as a varix or angioma, and fourth, because of hyaline degeneration in the firm hyaline node. These are all different phases of the same pathologic condition and are the result of vocal trauma. The elastic tissue forming the base of Reinke's space and overlying

the muscle may act as a barrier to the invasion of a cordal cancer, and this barrier, together with the lack of lymph spaces and nodes in Reinke's layer, may explain the late appearance of metastasis in cordal cancer. Dr. Cunning states that radiotherapy of early cordal cancer shows as good results as surgical removal of the growth. Cutler, Quick and Lenz, with their wide experience in radiotherapy, agree with the opinion expressed by Dr. Cunning. Dr. Cunning's courage in taking a stand on this controversial question is to be admired.

DR. JOSEPH I. KEMLER, Baltimore: In Baltimore my associates and I occasionally get good results, but not as good as those Dr. Cunning reported. In order to conserve the larynx, I recently devised an operation which is a little more radical than the ordinary laryngofissure and in many cases can take the place of a laryngectomy. With local or thiopental sodium anesthesia, a midline incision is made from the hyoid bone to just below the cricoid cartilage. The thyroid cartilage is exposed without dissection of the flaps, and the external perichondrium is incised in the midline and dissected laterally for 1 cm. on each side. The cartilage is then incised vertically on each side at this distance from the midline. These incisions extend to, but do not divide, the inner perichondrium. With the Freer elevator the inner perichondrium, unopened on the involved side, is now separated from the medial surface of the remainder of the ala of the thyroid cartilage to the arytenoid. On the uninvolved or lesser involved side, this separation of the inner perichondrium is either omitted or carried out, depending on the location of the tumor. A horizontal incision is then made through the cricothyroid membrane at the upper border of the cricoid cartilage. This incision is directed vertically through the inner perichondrium and the laryngeal mucosa of the freed uninvolved or lesser involved side to the top of the larynx. The incision is again directed horizontally toward the opposite side, passing above the thyroid notch. The freed tissue, which includes a 2 cm. strip of anterior thyroid cartilage, the inner perichondrium and the mucosa of the uninvolved side, is swung like an opening door toward the involved or more greatly involved side, and the interior of the larynx is then exposed. This entire mass is cut out. The cartilage on the involved side is completely denuded, and the arytenoid may also be denuded if necessary. On the uninvolved or lesser involved side a part of the cord remains in situ. The wound is closed by suturing of the outer perichondrium and the muscles, the skin being sutured separately.

DR. HENRY M. SCHEER, New York: A discussion of carcinoma of the larynx is always timely, and Dr. Cunning has given a comprehensive presentation. Nevertheless, I feel that, unless we leave this meeting with little or no confusion as to therapy, we have not gained much. As one of the previous discussers mentioned, laryngologists should have the courage to take a stand. Dr. Cunning has stated that, in early cordal carcinoma, radiotherapy should be applied. I am of that group that has seen early carcinoma of the vocal cords successfully treated over thirty years by such radiologists as Dr. Lenz and Dr. Quick. One of the recent cases is that of a physician, 86 years of age, with a cure now of five years' duration. It is unfortunate that this type of paper is most frequently presented before otolaryngologists. I feel that the general practitioners should hear this paper, because it is they who see these early lesions, who diagnose them and who, unfortunately, cause delay by referring the patients to us when the lesions are well developed and require surgical intervention. The early cordal lesions are missed. I disagree with Dr. Smith that the medical student should have thorough training in the examination of the larynx. They do not have the time. Members of every branch of medicine advocate the same thing. They say that the medical student should study cancer of the genitourinary and gastrointestinal tracts, the pulmonary system and so on. The student does not have the time to get specialized training in each branch. It is up to the specialists in the various fields to train the intern, to train the resident and to train the general practitioner. The general practitioner can be trained, and, if he is trained, many patients with early lesions will be saved from operative intervention by radiotherapy. There are capable men all over the country who can apply this therapy. It is not confined to New York City. If laryngologists impress those who see these cases early, general practitioners, they will accomplish something and will not cause confusion with respect to roentgen therapy.

DR. MAURICE LENZ, New York: Treatment of cancer of the larynx should be by cooperative effort of the laryngologic surgeon and the radiotherapist. The latter should be able to make laryngoscopic examinations, since roentgen dosage is varied in accordance with daily laryngologic changes. The results of roentgen therapy are influenced by the location and extent of the laryngeal involvement and by the presence or absence of metastatic regional lymph nodes. Results are best in small papillary cancers arising on the vocal cords or epiglottis; they are worse when the growth is extensive and deeply ulcerating. Results are poorest when the growth originates in the pyriform sinus. Prognosis is aggravated by the presence of metastatic lymph nodes. Roentgen therapy of cordal cancer limited to the middle of one cord gives as high a rate of cure and a better voice than laryngofissure. In more extensive cordal cancers roentgen therapy is as effective as laryngectomy, unless there is invasion of the arytenoid or of the subglottic region, in which cases laryngectomy is more reliable. In cases of failure of roentgen therapy, laryngectomy may be done without delay in postoperative healing. Roentgen therapy is the treatment of choice for cancer of the epiglottis. Metastatic neck nodes secondary to cordal cancer are preferably resected, whereas roentgen therapy is often successfully used in nodes secondary to epitheliomas of the band or epiglottis. Work in a joint follow-up clinic is the best method of learning the advantages and shortcomings of each method of treatment. I have worked in this way with Dr. Cunning at the Manhattan Eye, Ear and Throat Hospital for six years and with Dr. John Kernan at the Presbyterian Hospital for sixteen years. Such cooperative effort develops unbiased judgment as to the best treatment in the individual case and should be carried out wherever laryngeal cancer is treated.

DR. DANIEL S. CUNNING, New York: It has been my endeavor for years to fully stress the importance of early diagnosis in these cases, thus enabling the physician to ascertain at the earliest possible date the effectiveness of surgical intervention as against roentgen therapy. I was introduced to the use of roentgen therapy more or less by chance. I will admit that the roentgen treatments were used in the first 3 cases much against my will and because the patients refused laryngofissure. However, the results were so gratifying that I decided it would be wise to employ roentgen therapy in a large series of cases, which would necessitate close and detailed follow-up study. To the time of writing I have treated 19 patients in this manner, 18 of whom are alive and well. I plan to follow these cases from year to year and shall report the results to you at some later date.

Pulmonary Embolism.—In former years pulmonary embolism was usually considered a complication of surgery. It is now generally recognized that many patients who have never undergone surgery are at times troubled with venous thromboembolic disease and that these patients may suffer from a fatal attack of pulmonary embolism. Internists now correctly attribute certain chest complications as the result of pulmonary emboli in bedridden patients who have undergone surgery. Attention is also being called to the presence of the early signs of venous thrombosis in the extremities. Adequate therapy saves many patients from the unfortunate outcome which in previous years occurred.

The majority of venous clots have their beginning in the deep veins of the lower leg and foot. The thrombosis which begins in the plantar veins or in the deep veins of the leg may gradually extend to higher levels by direct propagation. In other instances such a clot may be dislodged before extensive propagation has taken place. In such instances fatal pulmonary embolism may occur and at autopsy the origin of the fatal embolus will not be found unless the veins of the lower leg are examined.—Harwell Wilson, M.D., Surgery for the Prevention of Pulmonary Embolism, *The American Journal of Surgery,* October 1949.

ACUTE PANCREATITIS

A Clinical Study

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and
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The clinical manifestations of acute pancreatitis have been studied in a group of 98 patients admitted to the Cincinnati General Hospital during the years 1941 to 1948 inclusive. Since some patients were admitted more than once with the same diagnosis, a total of 111 admissions was available for analysis. The diagnosis for each admission was based on at least one of the following criteria: (1) a consistent clinical history in conjunction with an elevated serum amylase level; (2) surgical observations, and (3) postmortem examination. In each case that was analyzed acute pancreatitis was considered to have been the chief or a major factor in the illness.

A complete review of the subject of pancreatitis, including the etiology, pathology, diagnosis and treatment, has recently been discussed elsewhere by us.[1]

CLINICOPATHOLOGIC TYPES

The disease of acute pancreatitis, a loose clinical term, included three general clinicopathologic types which could be differentiated by clinical characteristics and by gross pathologic observations.[2] The commonest form was acute interstitial (edematous) pancreatitis, a relatively benign condition, usually self limiting and only occasionally fatal. It was identified grossly at surgical operation or at postmortem examination by induration and swelling of the pancreas without evidence of softening or hemorrhage. In the absence of anatomic verification, a patient with acute pancreatitis was arbitrarily placed in the interstitial classification if the clinical course was benign or if there was no clinical evidence of hemorrhage, necrosis or suppuration within and about the pancreas. Hence, the interstitial group, 74.8 per cent of the 111 cases, included not only patients with the anatomic lesion of acute interstitial pancreatitis but also those in whom the disease, lacking an anatomic classification, followed a benign, uncomplicated clinical course. The most dramatic form of the disease was acute pancreatitis with hemorrhage and necrosis (acute hemorrhagic pancreatitis, acute pancreatic necrosis). All cases in this group, 11.7 per cent of the total series, were verified by operative observation or necropsy. Clinically, acute pancreatitis with hemorrhage and necrosis tended to be rapidly fatal. The category of acute pancreatitis with suppuration or pseudocyst (acute suppurative pancreatitis) included cases diagnosed at operation and necropsy as well as those in which there were clinical signs of an intra-abdominal abscess or pseudocyst following an attack of acute pancreatitis. This group amounted to 12.6 per cent of the total series. Only 1 admission, a fatal case lacking postmortem examination, could not be classified as to clinicopathologic type according to the criteria established (table 1).

Age Incidence.—Acute pancreatitis was found to affect persons in all decades. Over one half of the patients (57.6 per cent) were younger than 51 years, but the importance of acute pancreatitis as a disease of advanced age was illustrated by the relatively high proportion (16.2 per cent) of patients in the seventh decade. About 40 per cent of the patients in the hemorrhagic group were over 70 years of age. Advanced age did not seem to be a factor affecting fatality in this series (table 2).

Sex and Race.—Females constituted 58.6 per cent of the cases. The higher incidence of acute pancreatitis among females may have been related to the fact that associated gallbladder disease occurred two times more frequently among the females. No unusual race distribution was observed. White patients amounted to 59.4 per cent, and the remainder were Negroes. This ratio approximated the racial distribution among the general admissions to the Cincinnati General Hospital (table 3).

TABLE 1.—*Clinicopathologic Types of Acute Pancreatitis*

Type	Patients, Number	Admissions	
		Number	per Cent
Interstitial (edematous)	71	83	74.8
Hemorrhagic (necrotic)	13	13	11.7
Suppurative (pseudocystic)	13	14	12.6
Unclassified	1	1	0.9
Totals	98	111	100.0

TABLE 2.—*Age Distribution in 111 Cases of Acute Pancreatitis*

Years	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80
Cases	1	4	14	28	17	16	18	13
Per cent	0.9	3.6	12.6	25.2	15.3	14.4	16.2	11.7

TABLE 3.—*Sex, Race, Mortality and Operative Mortality According to the Clinicopathologic Type of Acute Pancreatitis*

	Interstitial, per Cent (83 Cases)	Hemorrhagic, per Cent (13 Cases)	Suppurative, per Cent (14 Cases)	Total Series, per Cent (111 Cases)
Males	42.2	38.5	42.8	41.4
Females	57.8	61.5	57.2	58.6
White	61.4	53.8	50.0	59.4
Negro	38.6	46.2	50.0	40.6
Mortality	4.8	84.7	28.6	18.0
Operative mortality	6.9	60.0	18.2	15.5
Incidence of operation	34.9	38.5	79.6	40.6

CLINICAL HISTORY

Although usually not diagnostic, the clinical features of a patient with acute pancreatitis frequently were sufficiently characteristic to permit a diagnosis of acute pancreatitis before the serum amylase level had been determined.

Predisposing Factors.—Detailed histories revealed that for months or for years many of the patients (41.4 per cent) had noticed indigestion of a nonspecific nature, consisting perhaps of intolerance to certain foods, of epigastric fulness after meals, of belch-

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Owing to lack of space this article has been abbreviated in THE JOURNAL by omission of portions of the clinical observations and data. The complete text will appear in the authors' reprints.

1. Siler, V. E., and Wulsin, J. H.: Pancreatitis, to be published.

2. Fitz, R. H.: Acute Pancreatitis, M. Rec. **35**: 197, 225 and 251, 1889. McWhorter, G. L.: Acute Pancreatitis, Arch. Surg. **25**: 958 (Nov.) 1932. Elman, R.: Acute Interstitial Pancreatitis, Surg., Gynec. & Obst. **57**: 291, 1933; Surgical Aspects of Acute Pancreatitis, J. A. M. A. **118**: 1265 (April 11) 1942.

ing and of vague dyspepsia with occasional relief with antacid medicaments. An even higher proportion of the patients (60.3 per cent) had experienced at some earlier date attacks of abdominal pain similar to that of the present illness. Usually the previous episode was described as having been milder, relatively transitory (lasting several hours to a day) and not accompanied with vomiting or fever. Although in some instances associated gallbladder disease may have been responsible for the symptoms referable to the upper part of the abdomen, it was probable that the majority of hospital admissions for acute pancreatitis had been preceded by milder bouts of the same disease.

Alcoholism.—Often described as a precipitating factor in acute pancreatitis,[3] alcoholism was noted in 8.1 per cent of the patients. Trauma[4] was an initiating factor in only 1 case, that of a girl aged 9 years who three days previously had been struck in the epigastrium by the handlebars of a bicycle. The termination of a normal pregnancy in 4 cases immediately preceded the onset of symptoms leading to an acute attack of interstitial pancreatitis. Although the relation between a postpartum state and an attack of acute pancreatitis was not clear, a diseased gallbladder may have been the link between the two conditions. Of the 4 patients, in 1 cholecystography revealed gallstones and in 2 others the gallbladder failed to fill properly (table 4).

Onset of the Present Illness.—In 87.3 per cent of cases the attack preceding hospitalization began with sudden, severe pain. This dramatic type of onset was slightly less common in the suppurative group, but of all the symptoms and signs in this series a painful sudden onset was the most constant. The onset occurred at all times of day, frequently during sleep, and in only a few instances followed a heavy meal. In 10 per cent or more of the cases, especially among the older age groups, the first symptom was either nausea and vomiting or a vague and insidious indigestion. However, sooner or later in the course of the illness every patient without exception experienced abdominal pain.

Pain.—Characteristically the pain was severe and steady (63.1 per cent), as opposed to the sharp, brief pangs of biliary colic or the intermittent surges of intestinal obstruction. Less frequently the pain was crampy and intermittent or dull and ill-defined, attributes which were in no way diagnostic. In over half the patients (53.2 per cent) the pain originated in the epigastrium, but because of a tendency to be prominent in other locations the pain of acute pancreatitis was often confused with that of other conditions. More than half of all the patients noted prominent pain in areas other than the epigastrium, either throughout the abdomen and flanks or occasionally in the chest and shoulders.

Other Symptoms.—The remaining symptoms were not as helpful diagnostically as was the type of pain. Vomiting occurred in almost four fifths of the cases (77.5 per cent) and was distinguished by certain traits which, although not specific, were suggestive of acute pancreatitis. The prompt appearance of vomiting following the onset of pain, the tendency to recur despite an empty stomach, the relatively low incidence of nausea (31.5 per cent), and the unremarkable nature of the vomitus, which if not recently ingested food was usually clear or bile-tinged fluid, were features suggestive of reflex emesis in response to pancreatic pain. Although massive hematemesis early in the course of the disease was not encountered except in the presence of an established peptic ulcer, several patients noted blood-streaked vomitus, such as might occur with superficial erosion of the gastric mucosa.

Constipation was not a prominent feature in this series (18.9 per cent). A certain number of patients (9.9 per cent) complained of diarrhea. Gross melena did not appear early in the disease, except with a concomitantly bleeding peptic ulcer (table 5).

TABLE 4.—*Predisposing and Associated Conditions and Complications According to the Clinicopathologic Type of Acute Pancreatitis*

	Interstitial, per Cent (83 Cases)	Hemorrhagic, per Cent (13 Cases)	Suppurative, per Cent (14 Cases)	Total Series, per Cent (111 Cases)
Predisposing and associated conditions				
Previous indigestion	39.8	46.2	42.8	41.4
Previous similar pain in upper abdomen	60.2	38.5	85.7	60.3
Gallbladder disease *	28.9	61.5	42.8	34.2
Gallstones †	24.1	53.8	42.8	29.7
Peptic ulcer	4.8	15.4	7.1	6.3
Alcohol	8.4	15.4	0.0	8.1
Postpartum	4.8	0.0	0.0	3.6
Trauma	1.2	0.0	0.0	0.9
Complication				
Recurrent attack	22.9	0.0	14.3	18.9
Gastrointestinal bleeding	10.8	38.5	21.4	16.2
Abscess, retroperitoneal	0.0	46.2	28.6	9.0
Abscess, lesser peritoneal cavity	0.0	23.1	42.8	8.1
Sudden fatal shock	2.4	23.1	0.0	4.5
Diabetes	1.2	15.4	14.3	4.5

* Proportion of total males with gallbladder disease, 21.7 per cent; of total females, 43.1 per cent.
† Incidence of common duct stones among cases examined at surgical operation and at necropsy, 9.7 per cent.

TABLE 5.—*Symptoms of Acute Pancreatitis According to the Clinicopathologic Type of the Disease*

Symptom	Interstitial, per Cent (83 Cases)	Hemorrhagic, per Cent (13 Cases)	Suppurative, per Cent (14 Cases)	Total Series, per Cent (111 Cases)
Pain in abdomen	100.0	100.0	100.0	100.0
Painful onset	90.3	84.7	79.6	87.3
Severe, steady pain	67.4	53.8	42.8	63.1
Epigastric pain	54.2	61.5	42.8	53.3
Pain in right upper quadrant	16.9	7.7	7.1	14.4
Pain in left upper quadrant	6.0	0.0	21.4	7.2
Pain in right lower quadrant	2.4	15.4	0.0	3.6
Radiation of pain	42.2	31.8	50.0	41.4
Nausea	31.3	31.8	28.6	31.5
Vomiting	78.3	84.7	64.3	77.5
Constipation	....	....	....	18.9

SALIENT PHYSICAL OBSERVATIONS

On admission to the hospital only one fourth (24.3 per cent) of the total series of patients had a temperature of 100 F. or above, and fever prior to admission was an infrequent complaint. The pulse tended to be high in the more serious cases. Whereas in only 42.2 per cent of the interstitial group the pulse rose to 90 or above, in 61.5 per cent of the hemorrhagic-necrotic group a similar elevation to 90 was found. The blood pressure at admission revealed hypertension more

3. Clark, E.: Pancreatitis in Acute and Chronic Alcoholism, Am. J. Digest. Dis. **9**: 428, 1942.
4. Naffziger, H. C., and McCorkle, H. J.: The Recognition and Management of Acute Trauma to the Pancreas, Ann. Surg. **118**: 594, 1943.

often than it did shock. The blood pressure was 140 systolic and 90 diastolic or higher in 26.1 per cent of all admissions, confirming the observations of Paxton and Payne.[5] The hypertension did not seem to be influenced by the age of the patient; the number of patients below 50 years of age was about equal to that above. The restlessness, so commonly provoked by severe pain, may have been partially responsible for raising the blood pressure.

Obesity was noted in over one third of all cases (38.7 per cent) and was especially prominent in patients with the more serious forms of the disease. Jaundice was detected either by clinical examination or by subsequent laboratory tests in 38.7 per cent of all cases. The cause of the jaundice could not be definitely settled, because more than one half of the icteric patients gave evidence of coexisting gallbladder disease. Probably one third to one half of the instances of jaundice resulted from a temporary occlusion of the common duct by swelling within the head of the pancreas, as has frequently been reported with chronic inflammation in that region.[6] In this series, 1 case of interstitial pancreatitis with fat necroses, established at exploratory laparotomy and confirmed by a high postoperative serum amylase value (1,030 units per hundred cubic centimeters[7]), carried the incorrect preoperative diagnosis of carcinoma of the head of the pancreas.[8]

TABLE 6.—*Physical Observations According to the Clinicopathologic Type of Acute Pancreatitis*

Observation	Interstitial, per Cent (83 Cases)	Hemorrhagic, per Cent (13 Cases)	Suppurative, per Cent (14 Cases)	Total Series, per Cent (111 Cases)
Temperature 100 F.+	22.9	38.5	21.4	24.3
Pulse rate 90+	42.2	61.5	50.0	45.1
Blood pressure 140/90+	27.7	23.1	21.4	26.1
Shock	4.8	53.8	14.3	12.6
Obesity	34.9	53.8	42.8	38.7
Jaundice	39.8	31.8	35.7	38.7
Abdominal tenderness	98.8	100.0	100.0	99.1
Epigastric	45.8	38.5	35.7	44.2
Right upper quadrant	39.8	31.8	14.3	35.1
Left upper quadrant	13.3	7.7	35.7	15.3
Right lower quadrant	7.2	15.4	0.0	7.2
Generalized	7.2	31.8	42.8	15.3
Muscle spasm	65.1	46.2	14.3	55.8
Diminished peristalsis	51.8	53.8	42.8	51.3
Abdominal distention	25.3	31.8	64.3	31.5
Abdominal mass	18.1	31.8	79.6	27.1
Cullen's sign	1.2	0.0	0.0	0.9

The significant physical observations centered about the abdomen. Abdominal distention, reflecting the presence of paralytic ileus, was noted in 31.5 per cent of the series and was especially prominent in prolonged serious cases, such as those with pancreatic abscesses. Abdominal tenderness was elicited in every case except 1. Usually the tenderness was diffuse, centering in the area of maximum pain and spreading radially to other areas of the abdomen and only rarely localized to one point. The commonest site of maximum tenderness lay in the epigastrium (44.2 per cent), but over one third of the patients (35.1 per cent) experienced maximum tenderness in the right upper quadrant of the abdomen. Tenderness in the left upper quadrant, often considered characteristic of pancreatitis, was found in 15.3 per cent of all cases. In some patients, such as those in whom abdominal masses had developed, the tenderness was minimal or was confined to the contour of the mass. In 7.2 per cent of the series maximum tenderness lay in the right lower quadrant, leading to erroneous diagnoses and unnecessary operations. Rebound tenderness accompanied direct tenderness in somewhat less than half of the cases. Abdominal muscle spasm was noted in two thirds of the interstitial cases but was less common in the suppurative and hemorrhagic types. On several occasions the entire epigastrium was rigid enough to be considered characteristic of a perforated peptic ulcer. Peristaltic sounds were noted to be diminished or absent in one half of the cases (51.3 per cent). This was believed to be a manifestation of a tendency to the development of paralytic ileus.

An abdominal mass, usually firm, fixed and tender, was palpated either on admission or later in the course of the disease in 27.1 per cent of the total series. Among the patients with interstitial pancreatitis a mass appeared less frequently, but when present it usually was detected in the right upper quadrant. About 80 per cent of patients with suppurative or cystic pancreatitis had abdominal masses, which lay predominantly within the left upper quadrant. About 30 per cent of the hemorrhagic-necrotic group showed abdominal masses, and all were located on the right side of the abdomen. Usually the palpable mass represented a true abscess or pseudocyst, but on several occasions it proved to be inflamed, matted omentum which was studded with multiple fat necroses. Cullen's sign[9] was noted in only 1 patient, who had severe hemorrhage and necrosis within the pancreas. A faint periumbilical ecchymosis was seen on admission, the sixth day of illness (table 6).

LABORATORY DATA

On admission no significant degree of anemia was noted. Leukocytosis was common and out of proportion to the admission temperature. In 83.8 per cent of the total series the white blood count on admission amounted to 10,000 or more; in 17.1 per cent it ranged from 20,000 to 30,000.

The most reliable single diagnostic point was an abnormal elevation of the serum amylase. When the number of units of amylase activity per hundred cubic centimeters of serum rose above 200, as determined in this hospital,[7] an abnormal elevation was indicated; this was noted in 82 per cent of all cases. As a rule, the test was repeated daily or every other day until consecutive normal values were obtained. The intensity of amylase activity bore no relation to the clinical or pathologic severity of the disease. Maximum values were usually obtained on the day of admission or shortly thereafter and were followed by a drop to normal over a period of several days. Despite the high degree of correlation between an elevated value of the serum amylase and the clinical picture of acute pancreatitis, this laboratory test was at times misleading. In 1 instance of acute interstitial pancreatitis proved at laparotomy and in a second case of rapidly fatal acute pancreatic necrosis, in which the lesion at necropsy

5. Paxton, J. R., and Payne, J. H.: Acute Pancreatitis, Surg., Gynec. & Obst. **86**: 69, 1948.

6. Walters, W.: Bile Duct Obstruction, Surgery **3**: 884, 1938.

7. The technic for the determination of the serum amylase consisted of a modification of Somogyi's saccharogenic method. Somogyi, M.: Micromethods for the Estimation of Diastase, J. Biol. Chem. **125**: 339, 1938.

8. Bisgard, J. D.: Pancreatitis as a Cause of Complete Obstruction of the Common Duct, Ann. Surg. **124**: 1009, 1946.

9. Fallis, L. S.: Cullen's Sign in Acute Pancreatitis, Ann. Surg. **106**: 54, 1937.

was confined to the head of the pancreas, normal serum amylase values were found in samples taken at approximately the forty-eighth hour of the acute illness.

The urine contained albumin in 39.6 per cent of all cases, and in well over half of the cases with severe lesions. Glycosuria, indicating transient as well as permanent diabetes, occurred in 7.2 per cent of the total series. It pointed to severe damage of the pancreas and was most commonly observed in the group with suppurative lesions. All patients with glycosuria were found to have had an associated hyperglycemia, as judged from fasting blood sugar levels and dextrose tolerance curves. The total incidence of hyperglycemia (9.9 per cent) amounted to twice the frequency with which permanent diabetes followed acute pancreatitis in this series (4.5 per cent).[10] Interpretation of electrocardiographic tracings, when taken, did not appear to aid in the diagnosis.

ROENTGENOLOGIC STUDIES

Immediately on admission the patients were examined roentgenologically with exposures of the abdomen in recumbent and upright positions. In no case of acute pancreatitis was free air observed within the peritoneal cavity. In 23.4 per cent of all cases a mild paralytic ileus, seldom severe, was observed; such observations on several occasions led to the wrong diagnosis of intestinal obstruction. Occasionally the radiologic evidence of calculi in the right upper quadrant diverted the clinician's attention from the pancreas, which was actually the seat of the acute illness. In the majority of instances these emergency roentenograms revealed nothing of significance.

Further roentgenographic studies within the course of the illness were often extremely valuable in aiding the physician to arrive at a precise diagnosis. By examination of the upper and lower gastrointestinal tracts with a contrast medium the radiologist was able in 17.1 per cent of all patients to demonstrate the effects of extrinsic pressure from abnormal enlargement in the region of the pancreas. Depending on the portion of the pancreas involved, various displacements of the adjoining viscera were noted, as described by recent authors.[11] Most commonly the stomach was displaced superiorly and anteriorly with frequent distortion of the antrum, while the duodenal loop was often widened. Lesions in the tail of the pancreas tended to depress the left half of the transverse colon. The early diagnosis of an extension of a pancreatic abscess to the left subphrenic space was made possible by visualizing the relation of the fundus of the stomach to the left side of the diaphragm after a swallow of barium had been administered to the patient, who was then tilted into a low Trendelenberg position.[12]

An effort was made to obtain cholecystograms by the Graham-Cole technic on all patients when the acute symptoms and any indications of jaundice had subsided. Of 41 patients so examined, only 17.1 per cent were considered to have normal gallbladders and in 31.7 per cent gallstones were visualized; in the remaining 51.2 per cent the gallbladder either was inadequately visualized or else functioned poorly. The accuracy of the cholecystogram appeared to be high, since in all 15 instances in which surgical operation or necropsy permitted subsequent verification the original roentgenographic impression was substantiated (table 7).

HOSPITAL OBSERVATIONS

Admission Diagnosis.—A correct admission diagnosis of acute pancreatitis was made in only 46.8 per cent of all cases, even with the available aid of the serum amylase test. Sources of error lay partially in a failure to determine the serum amylase level on admission of the patient and also in a tendency on the part of the admitting physician to discount an abnormal elevation after the test had been performed. One third of the incorrect diagnoses listed various diseases of the biliary tract as the chief diagnosis. Because of the nature of the pain and tenderness acute peptic ulcer, either penetrating or perforated, and acute appendicitis were also frequently incriminated instead of acute pancreatitis. The complete list of incorrect diagnoses included almost all the acute abdominal diseases.

TABLE 7.—*Laboratory and Roentgenologic Observations in the Clinicopathologic Types of Acute Pancreatitis*

Observation	Interstitial, per Cent (83 Cases)	Hemorrhagic, per Cent (13 Cases)	Suppurative, per Cent (14 Cases)	Total Series, per Cent (111 Cases)
Elevated serum amylase	89.2	53.8	71.4	82.0
White blood cells, 10,000+	86.7	69.2	78.6	83.8
Albuminuria	33.7	69.3	42.8	39.6
Glycosuria	2.4	15.4	28.6	7.2
Hyperglycemia	6.0	15.4	28.6	9.9
Ileus	21.7	31.8	28.6	23.4
Extrinsic pressure on gastrointestinal tract	6.0	23.1	79.6	17.1
Cholecystogram	43.4	7.7	28.6	36.9
Gallstones	....	....	....	(31.7)*
Poor visualization	....	....	....	(51.2)*
Normal	....	....	....	(17.1)*

* Percentage of total cholecystograms.

TABLE 8.—*Operations and Operative Mortality in 45 Cases of Acute Pancreatitis*

Operation	Number	Number of Deaths	Per Cent of Mortality
Exploratory laparotomy	9	2	22.2
Drainage of pancreatic abscess or pseudocyst	9	2	22.2
Incision and drainage of pancreas	5	2	40.0
Cholecystectomy with exploration of common duct	8	0	0.0
Cholecystectomy	2	0	0.0
Cholecystostomy	3	0	0.0
Exploration of common duct	2	0	0.0
Excision of pancreatic pseudocyst	1	0	0.0
Drainage of pericholecystic abscess	1	0	0.0
Drainage of left subphrenic abscess	1	0	0.0
Appendectomy	4	1	25.0
Totals	45	7	15.5

Associated Diseases.—Acute pancreatitis tended to afflict patients who were in relatively good general health. The over-all incidence in this series of proved gallbladder disease was 34.2 per cent, as determined at operation, at necropsy and by roentgenographic evidence of gallstones. If the criteria were broadened by also including those cases with only cholecystographic evidence of poor gallbladder function, the proportion of cases with probable gallbladder disease would rise to 48.6 per cent. Among the hemorrhagic and necrotic cases the proved incidence amounted to 61.5 per cent.

10. Shumacker, H. B., Jr.: Acute Pancreatitis and Diabetes, Ann. Surg. **112**: 177, 1940.

11. Glenn, J. C., Jr., and Baylin, C. J.: The Roentgen Findings in Acute Pancreatitis, Am. J. Roentgenol. **57**: 604, 1947. Metheny, D.; Roberts, E. E., and Stranahan, A.: Acute Pancreatitis, with Special Reference to X-Ray Diagnosis, Surg., Gynec. & Obst. **79**: 504, 1944.

12. Carter, B. N.: Left Subphrenic Abscess, Ann. Surg. **110**: 562, 1939.

Although the usual lesion was chronic cholecystitis, in 2 instances acute cholecystitis was observed. Gallstones in the gallbladder or common duct were found in 29.7 per cent of the entire series. A coincidental, active peptic ulcer of the duodenum or stomach was noted in 6.3 per cent of the total series. In 1 fatal case a large pancreatic abscess had formed at the site where a duodenal ulcer had penetrated into the gland. A minimum of the associated conditions usually found among patients in the older age groups appeared among those of this series. There were no proved deaths from coronary occlusion or cerebrovascular accidents (table 4).

TABLE 9.—*Gross Pathologic Anatomy in Acute Pancreatitis*

	At Operation, per Cent (45 Cases)	At Necropsy, per Cent (17 Cases)
Pancreas, partial involvement only	....	52.9
Gallbladder, normal	20.0	35.3
Gallbladder, diseased	42.3	64.7
Gallbladder, stones	31.1	58.8
Common duct, normal	20.0	58.8
Common duct, dilated	13.3	17.6
Common duct, stones	4.4	23.5
Peritoneal fluid, excess	26.7	47.1
Fat necrosis	24.2	76.5
Lesser peritoneal cavity (a) fluid	11.1	11.8
(b) abscess	11.1	23.5
Retroperitoneal abscess	8.9	35.3
Acute inflammaiton in peripancreatic structures	29.4*	84.7*

* Cases with suppurative pancreatitis excluded.

Operation.—In the face of a known diagnosis of acute pancreatitis an emergency operation was not performed. Those patients subjected to immediate surgical intervention represented either those whose disease was incorrectly diagnosed preoperatively or those in whom operative intervention was deemed necessary to establish a diagnosis. If the presence of known gallstones appeared to contribute materially to the acute illness, occasionally a cholecystostomy was performed as an emergency procedure. Subsequent to recovery from the acute attack, patients with proved cholelithiasis were urged to undergo elective cholecystectomy. In 1 instance this procedure was followed by a recurrent attack of interstitial pancreatitis during the immediate postoperative period.

TABLE 10.—*Bacteriologic Observations in 17 of 111 Cases of Acute Pancreatitis*

Organism	Interstitial, Cases	Hemorrhagic, Cases	Suppurative, Cases	Total Cultures
E. coli	0	1	4	5
A. aerogenes	0	0	1	1
Staph. aureus	0	1	2	3
Staph. albus	0	1	1	2
Hemolytic streptococci	0	1	0	1
Cl. welchii	0	1	0	1
Sterile cultures	1	0	6	7

Patients with fresh hemorrhagic or necrotic lesions tolerated operative intervention poorly. Especially poor results were noted after incision and drainage of the pancreas itself in an attempt to evaluate areas of recent pancreatic necrosis where there was no evidence of frank suppuration or liquefaction. In each of 3 cases so treated an extensive purulent abscess developed in the drained area during the second postoperative week, resulting in the ultimate death of 2 of the 3 patients. During the period of fever and acute inflammation the only surgical procedure that appeared to help the patient with acute pancreatitis consisted in the adequate drainage of abscesses and pseudocysts wherever the masses presented. On 1 occasion the operator was able to excise completely a pancreatic pseudocyst. The drainage of abscesses was always delayed until the patient had been properly prepared with supportive measures and until it had become evident that spontaneous resorption was unlikely. Because of an incorrect preoperative diagnosis four unnecessary appendectomies were performed as emergency procedures with the removal of relatively normal appendixes. This operation hindered the recovery of the patient and in 1 instance was followed by death (table 8).

Operative Mortality.—In the total series, 45 patients submitted to operation with an operative mortality of 15.5 per cent. Two deaths occurred in the interstitial group, but neither were attributable to pancreatitis. The operative mortality in 5 patients with hemorrhagic necrosis was 60 per cent. Within the suppurative and cystic group, in which the operations were limited to draining collections of fluid, the operative mortality was 18.2 per cent (table 3).

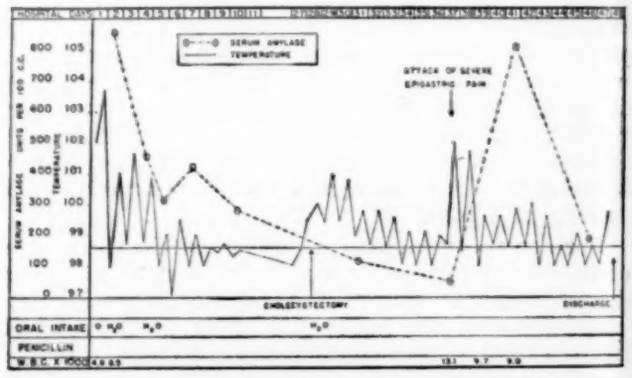

Fig. 1.—Acute interstitial pancreatitis (patient aged 18), typical in the satisfactory response to conservative measures without the use of penicillin. A brief recurrence after interval cholecystectomy also subsided spontaneously.

Total Mortality.—The total mortality of the entire series (18 per cent) was lower than that usually reported,[14] undoubtedly because with the increasing use of the serum amylase test the interstitial group was expanded by cases which formerly would not have been diagnosed as acute pancreatitis. The mortality within the interstitial group amounted to 4.8 per cent. Although this group was considered in general to follow a benign course, death occurred shortly after admission of 2 patients in whom the pancreas grossly showed only evidence of induration and swelling without hemorrhage or necrosis. The cause of death in these 2 cases was not clear, especially since other patients with similar pathologic lesions survived. In the group with proved hemorrhagic or necrotic lesions the mortality amounted to 84.7 per cent, a discouragingly high figure. For the group with suppurative lesions or pancreatic pseudocysts the mortality fell to 28.6 per cent (table 3).

14. Morton, J.: Acute Pancreatitis, Surgery **17**: 475, 1945. Lewison, E. F.: Acute Pancreatitis, Arch. Surg. **41**: 1008 (Oct.) 1940. Schmieden, V., and Sebening, W.: Surgery of the Pancreas, Surg., Gynec. & Obst. **46**: 735, 1928.

GROSS PATHOLOGIC ANATOMY

An opportunity to observe the pathologic anatomy of acute pancreatitis was offered in a series of 45 operations and 17 postmortem examinations. Since many of the surgical procedures, such as drainage of abscesses, offered a restricted view of the abdominal viscera, only limited conclusions could be drawn from negative observations.

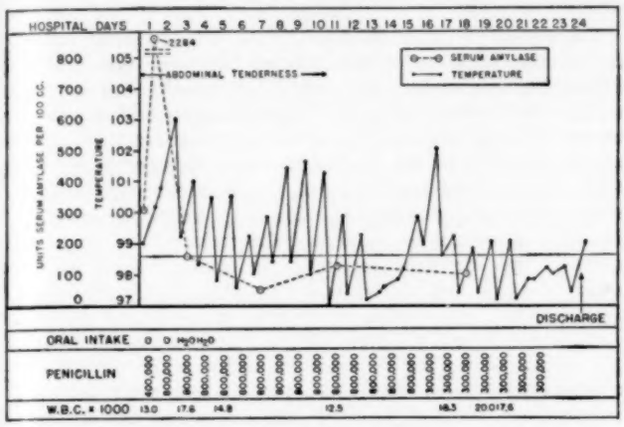
HOSPITAL DAYS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
SERUM AMYLASE
TEMPERATURE
ABDOMINAL TENDERNESS
DISCHARGE
ORAL INTAKE
PENICILLIN
W.B.C. × 1000

Fig. 2.—Typical case of acute interstitial pancreatitis (patient aged 76), in which morbidity was not significantly altered by the administration of large doses of penicillin.

A normal gallbladder was noted in 20 per cent of the operations and in one third of the necropsies. In the remaining instances the gallbladder either was chronically inflamed or contained stones. The incidence of stones in the common duct at operation and necropsy was 9.7 per cent. No stones were present in the ampulla of Vater (table 9).

Bacteriologic Data.—In 10 cases within this series, none from the interstitial group, cultures of material from the diseased pancreas were reported as being positive; in 5 of the 10 cases Endameba coli was recovered. On seven occasions cultures from the damaged tissues were reported as being sterile (table 10).

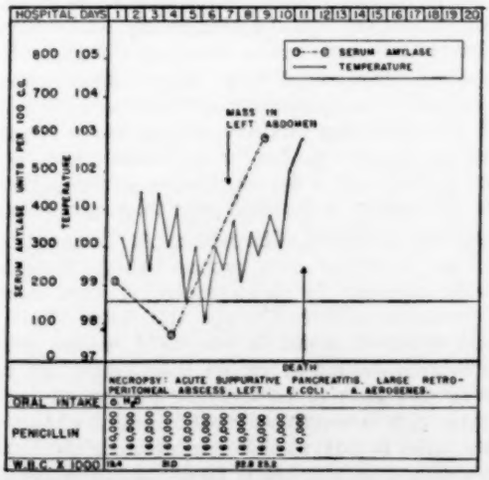
HOSPITAL DAYS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
SERUM AMYLASE
TEMPERATURE
MASS IN LEFT ABDOMEN
DEATH
NECROPSY: ACUTE SUPPURATIVE PANCREATITIS. LARGE RETROPERITONEAL ABSCESS, LEFT. E. COLI. A. AEROGENES.
ORAL INTAKE
PENICILLIN
W.B.C. × 1000

Fig. 3.—Acute suppurative pancreatitis (patient aged 61) in which a progressive and ultimately fatal retroperitoneal abscess developed despite the administration of penicillin.

NONOPERATIVE TREATMENT

During the acute phase of the disease, treatment consisted of nonspecific, conservative measures. All patients were put to bed on admission and were not allowed to ingest food or water during the first day or two until acute symptoms had subsided. Continuous aspiration of the stomach by means of a nasal gastroduodenal (Levin) tube helped to prevent vomiting, and it was believed that such a measure also assisted the course of the illness by preventing the acid gastric chyme from entering the duodenum and stimulating the flow of pancreatic juices. Narcotics and intravenously given fluids were administered as indicated. As soon as the abdominal pain and tenderness had disappeared, the patients were allowed to eat bland foods. In an attempt to avoid further recurrences after recovery from the acute attack, patients were advised to pursue moderation in eating and drinking and to continue treatment for such associated conditions as a diseased gallbladder or peptic ulcer.

Penicillin.—During the years 1946 to 1948 penicillin was administered to 28 patients with all types of pancreatitis in an attempt to prevent complications and improve morbidity. The course of patients with interstitial pancreatitis was not shortened and did not seem to be improved over those in the same group who did not receive penicillin (figs. 1 and 2). In this series there were no cases comparable to the 2 instances of acute streptococcic pancreatitis recently reported by Koller,[15] in which the use of penicillin would probably have been of great value. The usual dosage consisted of 20,000 units penicillin given intramuscularly every three hours. The use of penicillin in patients with suppurative or necrotic lesions as a rule did not produce striking improvement, although additional complications may have been prevented. One patient (fig. 3) who had been placed on a continuous dosage of penicillin (20,000 units intramuscularly every three hours) immediately on admission continued to have a fever; a large abdominal mass developed, and the patient died eleven days later with generalized peritonitis. Organisms recovered at necropsy from this abscess consisted of E. coli and Aerobacter aerogenes. In another patient who received penicillin following the drainage of a recent area of hemorrhagic necrosis in the pancreas a large and ultimately fatal abscess proceeded to develop at the site of drainage. Such examples did not lead to the abandonment of the use of penicillin in acute pancreatitis but merely suggested that this antibiotic drug could not be expected to cure the disease promptly and spectacularly.

SUMMARY

1. A clinical study has been made of 111 cases of acute pancreatitis seen at the Cincinnati General Hospital during the years 1941 to 1948. Diagnosis was based on one or more of the following criteria: (*a*) a consistent clinical picture in conjunction with an elevated serum amylase; (*b*) operative observations, and (*c*) postmortem examination.

2. The disease was considered to consist of three clinicopathologic types. Acute interstitial (edematous) pancreatitis, a relatively benign, self-limiting disease, was present in three fourths of the cases. Acute pancreatitis with hemorrhage and/or necrosis, a highly fatal disease with a strong propensity to develop serious complications, was identified at operation or necropsy in one eighth of the cases. Acute pancreatitis with suppuration or pseudocyst (acute suppurative pancreatitis), characterized by persistent abdominal masses

15. Koller, O.: Acute Interstitial Pancreatitis Provoked by Haemolytic Streptococci in Infected Food, Acta chir. Scandinav. **95**: 358, 1947.

and a prolonged acute illness, was noted in one eighth of the cases.

3. The age incidence was highest during the fourth decade but rose again to a secondary maximum in the seventh decade, indicating the importance of acute pancreatitis in advanced age as well as in early middle age. Distribution by sex and race was noted.

4. Predisposing factors, symptoms, physical observations, laboratory data and roentgenologic findings were analyzed for incidence within each of the clinicopathologic types, and the differences between the types were noted.

5. Of the entire series, 18.9 per cent of admissions were followed by recurrent attacks of acute pancreatitis. Associated gallbladder disease was present in 34.2 per cent of cases. The course, the complications, the pathologic anatomy as revealed at operation in 45 cases and at necropsy in 17 cases, and the bacteriologic studies were analyzed in relation to the types of acute pancreatitis.

6. The operative mortality for the entire series amounted to 15.5 per cent and for the hemorrhagic-necrotic group totaled 60 per cent. A total of forty-five operations was performed. Emergency operations were not undertaken in the face of an established diagnosis of acute pancreatitis. The only operative procedure of definite help during the acute illness consisted of incision and drainage of abscesses secondary to pancreatitis.

7. The total mortality (18 per cent) was lower than that usually reported in the past. The use of the serum amylase test showed that in many cases classified clinically as interstitial pancreatitis the disease pursued a benign course. Mortality for patients with interstitial pancreatitis was 4.8 per cent; with hemorrhage and necrosis, 84.7 per cent, and with suppuration or pseudocyst, 28.6 per cent.

8. Nonoperative treatment during the acute stage consisted of a conservative regimen of bedrest, of withholding food and water, of intravenous replacement therapy and of sedation. Penicillin, which was administered to 28 patients, did not appear to diminish morbidity in any striking manner.

ABSTRACT OF DISCUSSION

DR. ALTON OCHSNER, New Orleans: I regret exceedingly that Dr. Gage is not here; he could discuss the subject with considerable feeling, since he himself has had acute pancreatitis, which undoubtedly stimulated his intense interest in this interesting lesion. He has demonstrated to us that the therapy in acute pancreatitis should be conservatism. As Dr. Siler said, it consists of vasodilatation of the pancreas obtained by procaine (novocaine®) splanchnic block. In order to relieve the almost excruciating pain, which according to Dr. Gage could not be more severe, he employed splanchnic anesthetization; he believed that the beneficial effects might be only palliative relief of pain. However, we were astounded to observe not only that the patients are relieved of pain but that the progress of the disease is apparently stopped and the course is materially shortened. It is our belief that the progression of the lesion in acute pancreatitis is due to persistent spasm of the vessels within the pancreas and that by splanchnic block, which is done according to the technic of Kappis, prompt and dramatic relief of pain will be obtained and the progress of the disease with resultant necrosis can be prevented. Dr. Gage has had a series of 16 patients, in whom the diagnosis of acute pancreatitis was proved by the elevated serum amylase values, who have had splanchnic blocks. Mostly these patients have been subjected to surgical operation. Subsequently, all had gallstones and as determined by cholangiography all had a common opening of their pancreatic and common hepatic ducts, which permitted regurgitation of the bile into the pancreatic duct following temporary occlusion by the biliary calculus at the ampulla of Vater.

DR. ROBERT ELMAN, St. Louis: Dr. Siler's careful and well documented study has revealed many important aspects of this interesting disease and has emphasized several diagnostic and therapeutic lessons. He has rightly emphasized the importance of the serum amylase test, which was positive in 82 per cent of his cases at one time or another. This test is so important that accurate knowledge of the disease cannot be gained unless it is used as a routine. Dr. D. J. Verda has found that in many hospitals in St. Louis the incidence of acute pancreatitis has increased progressively, concomitantly with the more frequent use of the serum amylase test. Perhaps the best evidence of its value comes from some figures for which I am indebted to Dr. Samuel H. Gray of the Jewish Hospital, St. Louis, where for a period of many years routine blood amylase tests were made on every patient admitted to the surgical and medical services. This was due largely to the interest of Dr. Michael Somogyi, biochemist of the laboratory, whose method is now used almost entirely in this country. Their figures show that 1 of every 600 patients admitted had a high serum amylase value, indicating the presence of pancreatitis. This is a high incidence, about three or four times greater than that noted in any other hospital. It indicates that pancreatitis will undoubtedly be diagnosed much oftener when the serum amylase test is more frequently performed. In Dr. Siler's cases, despite his avowed program of early conservative therapy, reserving operative measures for definite indications later, about half of the patients were operated on, in many instances without knowing that the patient had pancreatitis, the diagnosis of some other intra-abdominal emergency having been made. If a serum amylase test had been done earlier, some of these operations might have been avoided. The one big unanswered question in the therapy of pancreatitis is whether to use operative or nonoperative therapy, once the diagnosis is made with the blood amylase test. I would like to emphasize that if all patients are treated conservatively, most will recover; all physicians have seen them recover with a variety of therapy or none at all. However, if this dogmatic attitude is adopted, certain patients will subsequently die of this disease. To save some of these patients, I believe that operation is necessary, and Dr. Siler has shown what can be accomplished, but results will not be good unless the surgeon sees these patients from the start. Too often he is called when the patient is moribund.

DR. VINTON E. SILER, Cincinnati: At Cincinnati General Hospital we have not used procainization of the regional sympathetic ganglions in the treatment of acute pancreatitis as has been advocated by Popper and Gage. This subject has been up for discussion in our ward rounds and in our surgical conferences, but as yet we have not felt the necessity of utilizing this form of conservative therapy. I agree with Dr. Ochsner that in severe acute pancreatitis the blood calcium level may fall. It may reach a critical level, and tetany may develop. Unquestionably this condition indicates that the patients should receive calcium therapy. Patients with acute pancreatitis are still surgical patients and must be observed by the surgeon. Patients in whom symptoms suggest a diagnosis of hemorrhagic pancreatitis are frequently difficult to manage, and the need of operative treatment in many of them as a life-saving measure is not easy to decide. The policy at Cincinnati General Hospital during the past five years has been one of ultraconservatism in this group of patients, and surgical measures have been utilized only when there has been a positive diagnosis of a collection of fluid in the peritoneal cavity or of pancreatic pseudocyst. Following this regimen has lowered the mortality rate in this pathologic entity.

GANTRISIN® IN THE TREATMENT OF URINARY INFECTIONS

GRAYSON CARROLL, M.D.
HOLLIS N. ALLEN, M.D.
and
HELEN FLYNN, M.S.
St. Louis

The development of new and potent agents for the control and treatment of infection holds much promise for the medical profession. This is particularly true in view of the rapidity with which new antibiotics are being made available. The promise or hope contained in each new drug cannot, however, be properly evaluated unless physicians first learn where it can be expected to be of value, how it should be used and why they should use that particular agent in a given situation. In addition, the toxicity of the drug must be determined in order to weigh the disadvantages against the advantages of its use.

The evaluation of any chemotherapeutic agent for the treatment of urinary infections must be based on two premises. The first premise concerns obstruction of the urinary tract. This obstruction, regardless of degree, is the all important factor and must first be defined and relieved if chemotherapy is to be attended with any success. The second premise is that there is no available drug which will inhibit or destroy all the organisms causing urinary infection. Each of the agents now employed in the treatment of infection has its own antibacterial spectrum. We determine which drug to use by first identifying the infecting organism and then selecting the agent which, on the basis of in vitro tests, should be effective against that specific organism. We do not believe in a haphazard approach to the problem.

This report describes our experience in the evaluation of a new sulfonamide drug, gantrisin® (3,4-dimethyl-5-sulfanilamido-isoxazole).[1] This drug has also been reported in the literature under the experimental designation NU-445. Our program was divided into the following phases: first, the testing in vitro of various organisms to determine their sensitivity to gantrisin®; second, the clinical use of this drug in the treatment of urinary infections, after identification and testing in vitro of the offending organism; third, the correlation of the findings in vitro and in vivo, and fourth, our over-all evaluation of gantrisin® based on the previous three points and on our observations on the toxicity of the drug.

STUDIES IN VITRO

When studies are made in vitro, it becomes apparent that there are certain strains within a species that are resistant to the drug being tested. This resistance may persist even though the majority of the organisms are inhibited. For example, this is true to some degree of penicillin and more so of streptomycin. This resistance may also be enhanced by continually subjecting the organism to sublethal doses of penicillin or streptomycin. The naturally occurring variation in strains of a species makes it more desirable to conduct sensitivity tests in vitro than merely to identify the invading organism. We have performed such studies with gantrisin®; they are reported in detail elsewhere.[2] Since such sensitivity tests are not readily performed in many laboratories, it is of more practical value at the moment to limit the discussion of our results to the definition of those organisms which we have found to be generally inhibited by gantrisin.®

Our studies in vitro on 131 strains of various organisms indicated the following degrees of sensitivity to gantrisin®; the organisms are listed in the order of their decreasing sensitivity: Proteus, Alcaligenes, Escherichia coli, paracolon bacillus, Escherichia intermedium, Aerobacter aerogenes, Streptococcus fecalis and Pseudomonas.

These studies in vitro consistently demonstrated that Proteus was highly sensitive to gantrisin.® This is significant, since in our studies Proteus was found to be highly resistant to aureomycin, and only about 50 per cent of Proteus organisms were sensitive to streptomycin.

Pseudomonas proved to be the least sensitive of all the organisms tested with gantrisin,® since it required concentrations of more than 40 mg. per cubic centimeter to inhibit growth.

Our findings in vitro confirm in general the antibacterial spectrum of gantrisin® as previously reported by Schnitzer and co-workers[3] and by Rhoads and associates.[4] The differences in actual figures for sensitivities in vitro in their reports and ours can be explained on the basis of differences in the culture mediums and technic.

STUDIES IN VIVO

Cultures of the invading organisms were made and their sensitivity to gantrisin® determined. The patients were seen either daily or every two or three days. During each visit the patients were questioned concerning the symptoms of their urinary infection, and special note was made of any untoward reactions to gantrisin.® Microscopic urinalysis was made on each visit, and if the urine appeared clear a culture was made. We attempted to obtain at least two successive negative cultures, one of which was taken a few days after discontinuance of the drug. In addition, complete hemograms and nonprotein nitrogen determinations were secured.

During the initial phases of this program the dosage used was 1 Gm. of gantrisin® every six hours for twenty-four hours. Encouraged by the absence of toxic symptoms we later increased the dose to 2 Gm. every six hours. The patients received no concomitant alkali, and no special effort was made to force fluids, although records were kept of fluid intake and output. A few patients who were too ill to tolerate oral medication were given gantrisin® intramuscularly or intravenously. This was facilitated by the high solubility of the drug, which permitted the use of a solution containing a 40 per cent concentration of gantrisin.® In patients whose symptoms did not improve or in whom the gross appearance of the urine did not improve after a week of gantrisin® therapy, treatment was considered to have failed.

A summary of our clinical experience is presented in table 1. There were 13 cases of mixed infections.

These studies were made at St. John's Hospital, St. Louis.

Assistant Professor, Department of Urology, St. Louis University School of Medicine (Dr. Carroll); Pathologist, St. John's Hospital (Dr. Allen).

Read before the Section on Urology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1949.

1. Supplies of gantrisin® were made available for this study by Dr. M. J. Schiffrin of Hoffmann-LaRoche, Inc.

2. Carroll, G.; Allen, H. N., and Flynn, H.: Urologic and Cutaneous Review, to be published.

3. Schnitzer, R. J.; Foster, R. H. K.; Ercoli, N.; Soo-Hoo, G.; Mangieri, C. N., and Roe, M. D.: Pharmacological and Chemotherapeutic Properties of 3,4-Dimethyl-Sulfanilamido-Isoxazole, J. Pharmacol. & Exper. Therap. **88**: 47, 1946.

4. Rhoads, P. S.; Svec, F. D., and Rohr, J. H.: Clinical Evaluation of a New Sulfonamide: Gantrisan, Quart. Bull., Northwestern Univ. M. School **23**: 104, 1949.

In 7 of these cases the infection was caused by Pseudomonas and one or more other organisms. In such mixed infections, the organism sensitive to gantrisin® (e. g., Escherichia coli) disappeared with gantrisin® therapy, but the Pseudomonas remained. When the Pseudomonas infection was accompanied by infection with another organism that was relatively resistant to gantrisin® (e. g., Streptococcus fecalis), neither organism disappeared after treatment. In only 1 of the 13 cases of mixed infections was a completely negative culture obtained after gantrisin® therapy.

In confirmation of the studies in vitro, gantrisin® was effective clinically in 4 of 5 cases in which the infection was caused only by Proteus. The 4 patients with mixed Proteus and Streptococcus fecalis infection did not respond to gantrisin® therapy.

TABLE 1.—*Clinical Results with Gantrisin® in the Treatment of Urinary Infections*

Organism	No. of Cases	Negative Culture	Positive Culture
Escherichia coli	26	24	2
Proteus	9	4	5*
Alcaligenes	3	2	1
Paracolon bacillus	3	2	1
Escherichia intermedium	4	0	4
Other intermediate organisms	4	3	1
Aerobacter aerogenes	7	3	4
Streptococcus fecalis	10	1	9
Pseudomonas	16	4	12

* Includes 1 case of infection due to Proteus and 4 cases of mixed infection due to Proteus and Streptococcus fecalis.

TABLE 2.— *Correlation of Studies in Vitro and in Vivo*

Organisms	Sensitivity in Vitro Mg./Cc.	Clinical Effectiveness Negative Cultures, Percentage
Proteus	1.3 : 5	44
Escherichia coli Intermediate organisms Alcaligenes	1.3 : 10	87
Aerobacter Intermediate organisms Paracolon bacillus Escherichia coli	10 : 20	47
Pseudomonas Streptococcus fecalis	20 : 40	19

CORRELATION OF IN VITRO AND IN VIVO STUDIES

While the sensitivity of the infecting organism in the test tube was not an absolute guide to the clinical effectiveness of gantrisin,® there was relatively good correlation of these data. Table 2 summarizes these data.

The trend was consistent except with respect to Proteus. As has been previously noted, 4 out of 5 cases in which treatment failed involved mixed Proteus and Streptococcus fecalis infections. If we had used those cases in which the infection was due only to Proteus, the clinical effectiveness would be calculated as 80 per cent rather than 44 per cent. The higher figure would be more consistent with the trend.

We obtained no evidence of the development of increased resistance on the part of the organisms to gantrisin.® This was true both in vitro and clinically. This is in definite contrast to our experience with the other sulfonamide drugs and with streptomycin.

TOXICITY

Nausea, allergic reactions, increased nonprotein nitrogen and anemia were not experienced in this group of patients after the use of gantrisin.® Despite the fact that alkali was not given and no attempt was made to force fluids, the drug did not cause the formation of concretions and there was no decrease in urine output. Our entire experience with this drug has been characterized by the absence of toxic symptoms.

These observations, indicating the low toxicity of gantrisin,® are in agreement with those of earlier reports, which showed that the drug is soluble in acid mediums[5] and is well tolerated in therapeutic doses without the concomitant use of alkali or forced fluids.[5]

COMMENT

We have confirmed in general the antibacterial spectrum of gantrisin® as reported by previous workers.[6] Our clinical results with this drug are in agreement with results in a number of earlier reports on its use in urinary infections.[7]

We are of the opinion that gantrisin® is the drug of choice in the treatment of Proteus infections, since Proteus is not highly sensitive to any of the antibiotics. Indeed, gantrisin® was found to be effective in some cases of infection which had become resistant following streptomycin therapy. The usefulness of gantrisin® in the treatment of urinary infections due to Escherichia coli and Alcaligenes has been amply demonstrated.

The attractive features of this drug are enhanced by its low toxicity. It may be administered orally or parenterally without systemic or local reactions. The fact that it is a single sulfonamide drug of high solubility is an important consideration. When combinations of the sulfonamide drugs are employed in an attempt to achieve such solubility, there is always the chance that an allergic reaction might occur. In such a case, there is no way for the physician to know which of the drugs in the combination is the offending agent. This dilemma can be avoided by the use of a single sulfonamide drug of high solubility, such as gantrisin.®

SUMMARY

1. A study has been made of the sensitivity of various organisms to gantrisin® (3,4-dimethyl-5-sulfanilamido-isoxazole), both in vitro and in vivo.

2. Gantrisin® is the drug of choice in the treatment of urinary infections due to Proteus.

3. It is effective in the treatment of urinary infections due to Escherichia coli, Alcaligenes and certain intermediate organisms.

4. It is moderately effective in infections caused by Aerobacter and paracolon bacillus.

5. Infections due to Pseudomonas and Streptococcus fecalis are resistant to treatment with gantrisin.® In 5 of 26 such cases the infection responded favorably.

6. Gantrisin,® when given in therapeutic doses (2 Gm. orally every six hours or the intravenous or intramuscular injection of the 40 per cent solution), does not produce any local or systemic toxic reactions.

7. The concomitant use of alkali or forced fluids is not necessary.

5. Sarnoff, S. J.: Suggestions Regarding Management of Severely Affected Kidneys, M. Clin. North America **32**: 1415, 1948. Rhoads, Svec and Rohr.[4]

6. Schnitzer and co-workers.[3] Rhoads, Svec and Rohr.[4]

7. Rodgers, R. S., and Colby, F. H.: A Clinical Evaluation of a Recent Sulfonamide: NU 445, J. Urol. **59**: 659, 1948. Narins, L.: The Treatment of Bacillus Coli and Bacillus Proteus Infections of the Urinary Tract with a New Sulfonamide (NU 445), J. Urol. **59**: 92, 1948. Sarnoff, S. J.; Freedman, M. A., and Hyman, A. A.: The Treatment of Bacillus Proteus Infections with NU 445, J. Urol. **55**: 417, 1946. Lazarus, J. A.: Suggestions Regarding Management of Severely Affected Kidneys, M. Clin. North America **32**: 1415, 1948. Haines, W. H., and Miceli, S.: Some Observations on the Management of B. Proteus Infections of the Urinary Tract, Pennsylvania M. J. **50**: 1328, 1947.

CLINICAL RESPONSE OF THE TUBERCULOUS URETER TO STREPTOMYCIN THERAPY

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Augusta, Ga.

With the effective antibiotic activity of streptomycin in the treatment of tuberculosis of the urinary tract now established, it would seem that the conversion of the bladder urine from positive to negative for tubercle bacilli could be interpreted as a favorable response to the drug. However, this may not always be true when there has been long-standing involvement of the ureter. Prior to the advent of streptomycin, it was known that the ureter and bladder could recover from tuberculosis, while the renal parenchyma probably could not. An attempt at healing in the ureter by granulation, with resulting scar formation and subsequent stricturing, was the rule. Complete occlusion of the ureter was not uncommon, occurring in 10 to 20 per cent of cases, though it probably remained permanently occluded in less than 1 per cent. In an analysis of cases, it seemed to be more than a coincidence when my associates and I found five of six kidneys with old tuberculous lesions in which the ureter had become occluded or impassable after streptomycin therapy. The following tabulation shows the type of lesion and its duration in the aforementioned cases and in one case mentioned by Nesbit and Bohne.[1]

Type of Lesion	Duration, Months
Impassable stricture	5
Occlusion	2½
Occlusion	5
Occlusion	17
Occlusion, renal pelvis	5
Impassable stricture [1]	3

It is reasonable to assume that this is a manifestation of the healing process promoted by the streptomycin therapy. We found that during and after treatment passable strictures tended to tighten and become impassable, and in some cases there was occlusion. Such obstructions of the ureter may mislead the clinician by causing false negative reactions of the bladder urine by exclusion rather than healing of the tuberculous lesion.

Dr. Edgar Pund of the department of pathology, who examined the surgical specimens from the patients who had been treated with streptomycin, believes that the granulation tissue is healthier and richer in blood supply and that there is less tendency to caseation in these patients as compared with untreated patients. Tubercle bacilli may still be present, though less numerous in some specimens.

A guinea pig test elicited a positive reaction in all lesions referred to as positive in this report.

REPORT OF CASES

CASE 1.—A white woman 38 years of age had old lesions of both kidneys and ureters (figs. 1 and 2). The bladder showed a persistently negative reaction for bacteria within five months from the time the drug was started, which seemed incredible in a patient with lesions of this type. Studies revealed that the communication between the left renal pelvis and the tuberculous process in the kidney had occluded, sealing the latter off from the urine excreted by the kidney and making the urine from the left side normal. The right ureter became occluded, causing the bladder urine to remain normal for five months; however, after five months it reopened and the urine again became positive for tubercle bacilli. Since the kidney had been destroyed during this time, it was removed. Urine from the left kidney has remained normal more than twelve months.

Bacteriologic Studies in Case 1

Date	Examination	Bladder	Right Kidney	Left Kidney
3/ 5/47	Direct smear	—	+	—
	Culture	—	..	+
	Animal inoculation	—	+	+
4/ 2/47	Culture	+	..	..
	Animal inoculation	+	..	..
6/21/47	Direct smear	—	..	..
	Culture	—	..	..
5/ 3/47	Culture	+	..	..
	Animal inoculation	+	..	..
7/23/47	Culture	—	..	..
	Animal inoculation	+	..	..
8/21/47	Direct smear	+	..	..
10/ 7/47	Direct smear	—	..	..
	Concentrate	—	..	..
	Animal inoculation	—	..	..
	Culture	—	..	..
12/ 1/47	Concentrate	—	..	..
	Culture	—	..	..
	Animal inoculation	—	..	..
12/ 4/47	Direct smear	..	..	—
	Culture	..	..	—
	Animal inoculation	..	..	—
12/30/47	Concentrate	—	..	..
	Culture	—	..	..
	Animal inoculation	—	..	..
2/ 4/48	Concentrate	—	..	..
	Culture	—	..	..
	Animal inoculation	—	..	..
2/27/48	Direct smear	+	..	..
	Culture	+	..	..
	Animal inoculation	—	..	..
3/ 2/48	Concentrate	..	..	—
	Culture	..	..	—
	Animal inoculation	..	..	—
4/ 9/48	Direct smear	—	..	..
	Concentrate	—	..	..
	Culture	+	..	..
	Animal inoculation	+	..	..
5/ 8/48	Animal inoculation	+	..	—
	Culture	+	..	—
6/ 1/48	Concentrate	+	..	—
	Culture	+	..	—
	Animal inoculation	+	..	—
7/ 6/48	Concentrate	—	..	—
	Culture	+	..	—
8/ 6/48	Direct smear	+	..	..
	Culture	+	..	..
	Animal inoculation	+	..	..
9/30/48	Direct smear	+	..	..
	Culture	+	..	..
11/19/48	Direct smear	—	..	..
	Concentrate	—	..	..
12/ 7/48	Direct smear	..	+	—
	Concentrate	..	+	—
	Culture	..	+	—
	Animal inoculation	..	+	—
1/ 7/49	Concentrate	—	..	..
	Culture	—	..	..

From the Department of Urology, University of Georgia School of Medicine, Augusta, and Battey State Hospital, Rome, Ga.

Read before the Section on Urology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1949.

Dr. Rufus Payne and Dr. Fred Crenshaw, of the Battey State Hospital, cooperated in the study of these cases. Mr. Jack Wilson and his staff of the Medical Arts Department of the University of Georgia School of Medicine prepared the illustrations.

1. Nesbit, R. M., and Bohne, A. W.: A Present Day Rationale for the Treatment of Urinary Tuberculosis, J. A. M. A. **138**: 937 (Nov. 27) 1948.

CASE 2.—A 38 year old man had an old unilateral involvement with a passable stricture in the lower end of the right ureter. His bladder urine became negative for tubercle bacilli two and one-half months after administration of streptomycin. Attempts at catheterization of the ureter at this time revealed an impassable, strictured area. After having been occluded, with all tests showing negative reactions, for two months, the ureter reopened and remained open thereafter, with the bladder urine containing tubercle bacilli. A pyonephrotic kidney was later removed.

CASE 3.—A 25 year old man had an extensive old involvement of the left kidney and ureter. His urine consistently contained tubercle bacilli until the seventeenth month after streptomycin therapy was started, when it became normal. He had not received any drug for three months prior to this time. The ureter was found to be occluded on attempted catheterization, and the urine remained normal for three months, at which time a nephrectomy was done. Tubercle bacilli were present in the surgical specimen.

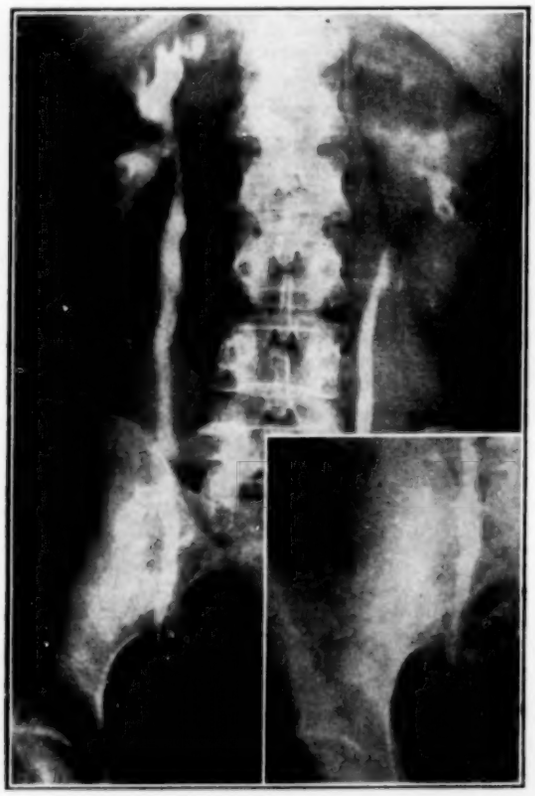

Fig. 1 (case 1).—Extensive old bilateral tuberculosis of the urinary tract before treatment. The increase in the constriction in the lower third of the right ureter followed treatment with streptomycin.

CASE 4.—A white woman, age 27, had tuberculosis of the left kidney and a long constricting involvement of the lower third of the left ureter. She received streptomycin for four months. The ureter was catheterized three times during this period in an attempt to keep it open, but by the fifth month an impassable stricture had developed. A pyonephrotic kidney was removed.

In the following case, the ureter improved during treatment, but I believe that it was a lesion in a much earlier stage and was not included in the group of old lesions.

CASE 5.—A white woman, age 27, whose first knowledge of illness was a hematuria, had miliary tuberculosis. Pulmonary lesions were found, and tuberculous meningitis developed a week after she was hospitalized. Attempted catheterization of the left ureter failed. An intravenous urogram showed ulceration of the minor calices on the left side, and the ureter was constricted and irregular in the upper third. After five months of streptomycin therapy, the ureter admitted a catheter easily. A pyelogram showed the lumen to be adequate, but it retained a characteristic stiffened appearance. It is noteworthy that the ureter improved, but the renal lesion above it progressed (fig. 3).

Fig. 2 (case 1).—An intravenous urogram showing only the lower major calix on the left, which had been negative for tubercle bacilli. Severe constriction of the renal pelvis with exclusion of the tuberculous process and involved calices may be seen. The right kidney is nonfunctioning, entirely destroyed by stricture in the ureter after administration of streptomycin.

Fig. 3 (case 5).—An intravenous urogram showing early involvement of the left ureter and ulcerative lesions of the lower, middle and upper minor calices of the left kidney prior to treatment. After treatment, the ureter is improved and the caliber is adequate, but there is characteristic stiffening. Renal tuberculosis is not improved.

Lattimer reported a case with a ureteral constriction, which he did not qualify, that improved after streptomycin therapy.[2] The tuberculous bladder contracts when the musculature becomes involved, and it would seem that the depth of the lesion might be the determining factor in the ureter. If the lesion is in an early stage and not too deep, resolution and healing without further constriction appear to take place.

CONCLUSIONS

In addition to making continuous tests for bacteria during and after treatment, one must also determine whether or not the urine from the tuberculous kidney is reaching the bladder. Bladder urine without tubercle bacilli in cases with ureteral involvement cannot be taken at face value without ureteral catheterization, chromocystoscopic study, with indigo carmine, or an intravenous urogram to prove that the ureter is open and draining into the bladder. Urine that does not contain bacilli because of a sealed off tuberculous process is misleading if it is not properly evaluated, as occluded ureters are apt to open later and result in bladder urine with bacilli (as occurred in a case in which there had been occlusion for as long as five months).

The possibility of further damage to the kidney above the strictured or occluded ureter has been demonstrated, and in some instances nephrostomy might be indicated to preserve the kidney. Early lesions of the ureter may regress, but healing in older and deeper lesions may result in increased contracture with a tendency to open later.

ABSTRACT OF DISCUSSION

ON PAPERS BY DR. RINKER AND DR. CARROLL, DR. ALLEN AND MISS FLYNN.

DR. E. CRAIG COATS, New York: Since the ureter is probably infected secondarily from a draining abscess in the kidney above and since the kidney is a poor medium for the growth of tubercle bacilli, the optimum time for streptomycin therapy is in the early stage, before deep-seated abscesses occur. The urologist seldom sees the patients at this stage. If the therapy does cause more rapid occlusion of the ureter during the healing process, physicians will be faced with the decision as to how best to protect the kidney from destruction by back pressure while attempting to cure it of tuberculosis. Diversion procedures will have to be used as the individual case dictates. A review was made of 167 cases seen on the Cornell Urologic Service at the New York Hospital prior to the advent of streptomycin. Forty-seven cases were selected for intensive study because, by cystoscopic, bacteriologic and roentgenologic evidence the patients had unilateral involvement and nephrectomy was performed. In none of these cases was complete ureterectomy performed, even though the ureter was involved. These cases were selected for study because it was believed that a recurrence of infection would probably start in the infected ureteral stump. The follow-up records, made over periods from two to fifteen years, fail to demonstrate that in any instance was it necessary to treat the ureteral stump further. However, 3 patients with normal urine and a normal urogram of the remaining tract had persistent frequency and dysuria for one, two and three years, respectively. They have remained well and free of any symptoms for two, five and fourteen years, respectively. Five patients had positive urinary reactions for long periods after operation. One had positive urine for one year, then was well, with normal urine for three years; 3 had positive reactions for six months and then were well, with normal urine for two, three and five years, respectively. One patient had a persistent loin sinus for two years. This finally healed, and, five years later, the patient has normal urine and normal urograms. One patient was well for twelve years, then experienced frequency and dysuria, although the urine and urograms were normal. It is this type of complication which will probably benefit most from streptomycin therapy. A judicious combination of streptomycin therapy and surgery should greatly increase the rate of cure.

DR. LOUIS C. ROBERTS, Durham, N. C.: We are indebted to Dr. Carroll for reporting a new nontoxic sulfonamide drug which gives promise of clearing up infections caused by certain organisms which have previously been resistant to all treatment. My own experience with gantrisin® has been limited. My associates and I treated a group of patients with infection due to Aerobacter aerogenes with this drug. Nineteen such patients were treated with gantrisin® with rather disappointing results. A number of these patients did respond so far as clinical symptoms were concerned. The amount of pus in the urine probably decreased, but in our group the urine was never culturally negative. In a number of cases the patients responded well so far as frequency of urination and other symptoms were concerned, but all of them had some recurrence of symptoms following discontinuance of the drug. Those who are familiar with Dr. Carroll's work in this particular field realize that his paper covers only a small segment of it.

DR. SEYMOUR F WILHELM, New York: Dr. Carroll has made an enormous contribution to our knowledge of the study and treatment of infection of the urinary tract. Especially important has been his insistence on making careful bacteriologic studies, both in vitro and in vivo, and on making frequent cultures of the urine, so that the proper chemotherapeutic agent or specific antibiotic substance can be used. My associates and I had difficulty two or three years ago in treating infection with Bacillus proteus following prostatectomy. We tested the efficacy of gantrisin,® then known as NU-445, and our results were published by our resident, Dr. Lester Narins (*J. Urol.* **59**:92 [Jan.] 1948). Our results agreed substantially with those reported by Dr. Carroll: in infection due to B. proteus the results were good; in infection due to Bacillus coli, they were fairly good but not as satisfactory. We found, also, that in infection due to Aerobacter aerogenes—we have observed many cases of infection due to this organism—this drug is of no clinical value, nor is it of any help in infections caused by Bacillus pyocyaneus. The drug was innocuous. There were few reactions and only occasional nausea. We saw no blood dyscrasias, febrile reaction or damage to the kidney. We felt at that time that gantrisin® was a valuable addition to the armamentarium for treatment of infections due to B. proteus and B. coli in a rather limited sense but that its effect was not as spectacular as that of some of the newer antibiotics, such as aureomycin. I have continued to use this drug in certain instances, and I think it is worth while.

DR. EDWARD COOK, Rochester, Minn.: Several things said by Dr. Carroll are worthy of emphasis. First, I would like to emphasize the good things he has said about gantrisin® (NU-445). These are the experiences of my associates and me with the drug. It has been innocuous. We have been able to give it to most patients without any difficulty. In only 1 patient did I see a serious reaction, and that patient had a dermatitis. The dermatitis had already developed a few months earlier, after the administration of one of the other sulfonamide drugs. Gantrisin® was given to see whether it would cause the same reaction. It did. The nausea, as Dr. Wilhelm said, has been present occasionally but has been minimal. I think that gantrisin® should become a definite part of the physician's armamentarium, because sometimes, when one of the sulfonamide drugs fails, another will succeed. Dr. Carroll brought out clearly the variations within the strains and within the particular species of organisms; these strains are not all the same. One infection due to Bacillus coli may be eradicated by sulfathiazole, and another may not. This does not mean that sulfathiazole is not of value in treating infections due to B. coli. The same holds for gantrisin,® mandelic acid, streptomycin, penicillin and aureomycin. In the treatment of infections of the urinary tract, the physician must never lose sight of the underlying pathologic conditions, because, in the presence

2. Lattimer, J. K., and others: The Streptomycin Treatment of Genito-Urinary Tuberculosis, J. Urol. **60**: 97 (Dec.) 1948.

of a stone, obstruction, tumor, foreign body or extensive pathologic changes, too much cannot be expected of these drugs.

DR. WILLIAM HERBST, Washington, D. C.: There is one factor concerning infection of the urinary tract which physicians should consider. That factor is general resistance. Except for the cases in which obstruction or foreign bodies are associated, infections of the urinary tract would not develop without poor general resistance. Sulfonamide drugs have been shown to reduce the elaboration of thiamine in the intestinal tract, thereby producing a relative deficiency. Therefore, all patients who are given sulfonamide drugs should be given vitamins. Vitamins are best given in adequate dosages. Dr. Carroll's data indicate that physicians have additional effectiveness from still another chemotherapeutic agent of the sulfonamide group.

DR. RALPH H. JENKINS, New Haven, Conn.: I would like to ask Dr. Rinker one question. Recently I saw a patient who had a tuberculous kidney removed several years ago, before the advent of streptomycin. Examination revealed that the other kidney was involved, with many strictures of the ureter. Should this patient be given streptomycin, since a stricture of the ureter might occur?

DR. GRAYSON CARROLL, St. Louis: The report on gantrisin® is a part of a larger study of antibiotic and chemotherapeutic agents which we have been making in relation to urinary infections. It is apparent that these agents have a selectivity for certain organisms and, therefore, should not be used haphazardly. The Proteus bacillus has proved highly resistant to most of the antibiotic agents. It would appear that this new sulfonamide drug, gantrisin,® will inhibit Proteus in low concentration. We advise its use in all infections due to Proteus. Escherichia coli, so commonly seen in urinary infections, is also inhibited in low concentrations, but unlike Proteus, it is inhibited by other antibiotics. However, gantrisin® would appear to be the drug of choice when E. coli is identified, because of its low toxicity and the ease with which it may be administered. The other sulfonamide drugs cause development of resistance in many organisms, but as yet this has not been noted with gantrisin.® Since the diethanolamine (*2,2'*-iminodiethanol) can be given in large doses (4 Gm. to 10 cc.) both intravenously and intramuscularly, high concentration can be obtained rapidly when the drug is given to patients with nausea. The organism most resistant to streptomycin encountered in our study is Pseudomonas, and, although 30 per cent of these organisms are initially inhibited by streptomycin, resistance develops rapidly. In our clinic this is the organism which has defied all the agents yet available. Careful identification and sensitivity tests are in order in all cases of recurrent or persistent urinary infections, and the physician should select the appropriate drug rather than just any antibiotic.

DR. J. ROBERT RINKER, Augusta, Ga.: Dr. Jenkins asked what should be done for a patient who has a single kidney with strictures of the ureter? That would depend on the degree of hydronephrosis demonstrated on the pyelogram. If it was increasing, I think that nephrostomy should be seriously considered. As I mentioned, in one of my cases I catheterized the ureter once a month just to see whether catheterization would keep it open. It did not, in that case. I believe you will agree that streptomycin therapy of tuberculosis of the urinary tract involves more than giving the drug and examining urine specimens.

Medical Philately.—The recently issued Grand Army of the Republic commemorative stamp indirectly is a tribute to a Springfield (Ill.) physician. Dr. Benjamin F. Stephenson, a graduate of Rush Medical College, Chicago (1850), was surgeon of the 14th Illinois Infantry during the Civil War, attaining the rank of major. He and the regimental chaplain, the Rev. William J. Rutledge, frequently discussed the idea of an organization of veterans and, after being mustered out, Dr. Stephenson furthered the plan. On April 6, 1866, he installed the officers of the first post at Decatur, Ill. Dr. Stephenson was made adjutant general until the national headquarters were moved to Washington, in 1867.

A PRINCIPLE FOR DETERMINING PROGNOSIS OF PREGNANCY IN RHEUMATIC HEART DISEASE

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and
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From the extensive literature on the subject of rheumatic heart disease in pregnancy, one concludes that several criteria may be used for selecting the good risks from the poor ones. Those most commonly cited are: the amount and degree of structural damage to the heart, the functional capacity of the heart, the size of the heart, the age of the patient, a history of antecedent congestive heart failure and the presence of auricular fibrillation.

There is, however, no agreement among authors as to the relative significance of each of these features. Moreover, some of the rules seem arbitrary and in general appear not to be related to one another.

For the past ten years we have had an opportunity to evaluate and test these criteria. We have found that there is a basic principle by which the prognosis of pregnancy in rheumatic heart disease may be determined, namely, by establishing the position which a given patient occupies in the natural course of rheumatic heart disease. The severest challenge to this principle arises from the question whether pregnancy itself may not significantly alter the course of rheumatic heart disease. If this were true, or even likely, the principle would become invalid. We believe, as will be demonstrated, that pregnancy does not seriously influence the natural history of the disease.

CLINICAL MATERIAL

A prenatal cardiac clinic was established at Bellevue Hospital in 1939 and has been conducted jointly by the Departments of Medicine and Obstetrics of the Third (New York University) Division.

Each patient included in this series was examined and studied by us.[1] The interval between visits varied from one week to one month, depending on the period of gestation and the cardiac status. Special attention was given to the history of rheumatic fever, and, when possible, reports were obtained from other hospitals and clinics concerning the patient's previous rheumatic manifestations and the course of her heart disease. The final cardiac diagnosis was made by the same observer (J. J. B.) in conformity with the criteria set by the New York Heart Association.[2]

From 1939 to 1948, 205 women were observed through pregnancy and puerperium. In 11 other cases pregnancy was interrupted because the prognosis was considered unfavorable.[3] In each of these cases sterilization was urged, for it was considered that a person who was already a poor childbearing risk would be unlikely to improve in this regard as her heart disease advanced.

Read before the Section on Obstetrics and Gynecology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1949.

From the Departments of Medicine and of Obstetrics and Gynecology of the New York University College of Medicine, and from the Third (New York University) Division of Bellevue Hospital.

1. A number of patients failed to attend the antepartum clinic and were seen by us for the first time at term on the obstetric wards. No patient with rheumatic heart disease delivered on our obstetric service was excluded from this series.

2. Nomenclature and Criteria for Diagnosis of Diseases of the Heart, ed. 4, New York, 1939, The New York Tuberculosis and Health Association,

3. During the four years preceding this study, from 1935 to 1939, 30 abortions were performed for patients with rheumatic heart disease.

The 205 patients were delivered of 209 babies. These included 6 mothers who gave birth to twins and 2 mothers who died undelivered. There were 122 spontaneous, 68 forceps and 9 breech deliveries. Cesarean section was performed on 6 patients for strictly obstetric reasons. We could see no indication to recommend this procedure on a cardiac basis. The presence of rheumatic heart disease is no longer acceptable as an indication for cesarean section. It may occasionally be resorted to as a means of terminating prolonged labor in order to reduce the danger of cardiac failure. Authors reporting their own results in groups of patients in whom cesarean sections were performed frequently as compared with those in whom it was done infrequently agree that the fatality rate is higher in the former group.[4] This may be attributed in part to the fact that those in whom childbirth presented the greater risks were more likely to undergo cesarean section. It is therefore important to note that among patients with heart disease of equal severity (classes 3 and 4)[5] the death rate is significantly higher in the group delivered abdominally (hysterotomy or cesarean section) than vaginally.[6]

OBSERVATIONS

Maternal Mortality.—Table 1 lists the maternal mortality rate from rheumatic heart disease reported in the literature from 1936 to 1948, inclusive. Reports prior to 1936 were not included because they had been collected and published by Jensen.[7] Those after 1936 show a striking reduction in mortality rates; from 9.38 per cent for the period 1890 to 1922 to 3.41 per cent from 1936 to 1948. This advance is probably a result of better understanding of heart disease and its treatment, more skilful and conservative obstetric management, closer cooperation between the obstetrician and the internist, and the advent of chemotherapy. Some reports, both foreign and American,[8] could not be included because the authors did not specify the type of heart disease among the total number of patients or among those who died, or both. It should not be assumed that all deaths listed were from rheumatic heart disease, since many writers made no distinction between the deaths resulting from the heart disease and those due to causes unrelated to it.

Of special interest is the report by Hedley[9] of a mortality rate of 18 per cent, which is strikingly higher than the others listed in table 1. Hedley reviewed the records of all women who died of rheumatic heart disease in pregnancy or puerperium in the general hospitals of Philadelphia from January 1930 to December 1934. He stated, "This discrepancy can largely be explained because of difference in the antenatal care. Most of the patients in this series who died were admitted in a serious condition and with little or no previous supervision."

TABLE 1.—*Reported Deaths Among Pregnant Women with Rheumatic Heart Disease, 1936 to 1948, Inclusive*

Authors	No. of Patients	No. of Deaths	% Deaths
Hay, J.: Post-Grad. M. J. **12**: 143, 1936	66	1	1.5
Hagedorn, W.: München. med. Wehnschr. **84**: 1246, 1937	50	5	10.0
Harris, K.*: Lancet **1**: 677, 1937	100	8	8.0
Lamb,[17a] 1937	102	7	6.9
McClure, H. J.: Ulster M. J. **5**: 234, 1936	69	3	4.3
Naish,[12a] 1937	427	11	2.6
Pardee, H. E. B.†: Am. J. Obst. & Gynec. **34**: 557, 1937	50	1	2.0
Carr, F. B.: New England J. Med. **219**: 231, 1938	44	1	2.3
Turino, T. R., and Antony, A. T.: Am. J. Surg. **41**: 453, 1938	102	6	5.9
Lange, F.: München. med. Wehnschr. **86**: 1557, 1939	322	6	1.9
Clahr, J.; Klein, M. D., and Greenstein, N. M.: New York State J. Med. **40**: 1242, 1940	181	4	2.2
Jensen, J.; Wegner, C.; Keys, E. H., and Smith, H. R.: Am. J. Obst. & Gynec. **39**: 443, 1940	108	8	7.4
Hedley,[9] 1940	116	21	18.1
Gorenberg and McGleary,[19a]‡ 1941	345	10	2.9
Bramwell, C., and Longson, E. A.: Heart Disease and Pregnancy, in Bramwell, C., and King, J. T.: Principles and Practice of Cardiology, London, Oxford University Press, 1942, pp. 216-230	312	22	7.1
Brown and Sage,[4b] 1942	32	1	3.1
Gorenberg, H.: Am. J. Obst. & Gynec. **45**: 835, 1943	223	8	3.6
Jones, A. M.: Post-Grad. M. J. **20**: 176, 1944	74	4	5.4
Sampson, J. J.: West. J. Surg. **51**: 107, 1943.	60	0	0.0
Mendelson,[6] 1944	1,089	8	0.7
Sutton, D. C.: M. Clin. North America **28**: 47, 1944	247	1	0.4
Scott, W. A.: Bull. Vancouver M. A. **21**: 78, 1944	114	3	2.6
Avilés, V. M.: Obst. y gynec. latino-am. **4**: 571, 1946	172	5	2.9
Henderson, D. N.: Am. J. Obst. & Gynec. **53**: 494, 1947	190	8	4.2
Evans, P. R. C.: Guy's Hosp. Rep. **96**: 194, 1947	85	8	9.4
Hamilton, B. E.: Am. Heart J. **33**: 663, 1947	1,244	47	3.8
MacRae, D. J.: J. Obst. & Gynaec. Brit. Emp. **55**: 184, 1948	212	7	3.3
Bunim and Appel,§ 1949	216	3	1.4
Totals	6,352	217	3.41

* Only deaths occurring within forty days post partum were included in this table.

† Three additional deaths due to subacute bacterial endocarditis, coronary thrombosis and "unspecified cause" occurred after discharge of patients from the hospital.

‡ The authors state that 95 per cent of the patients had rheumatic heart disease.

§ This group of 216 cases includes the 142 reported previously (Bunim, J. J., and Rubricius, J.: The Determination of the Prognosis of Pregnancy in Rheumatic Heart Disease, Am. Heart J. **35**: 282, 1948).

As will be noted, in our group there were 3 maternal deaths. One of our patients, 20 years of age, died of staphylococcic bacteremia during the fifth month of her first pregnancy. There was no discoverable focus of infection. The second patient, 33 years of age, died of heart failure in the ninth month of her seventh pregnancy. This patient was first seen by us at the end of her sixth pregnancy. At this time she manifested symptoms of diminished cardiac reserve, and sterilization was therefore advised. The patient did

4. (*a*) Hamilton, B. E., and Thomson, K. J.: Heart in Pregnancy and Childbearing Age, Boston, Little, Brown & Company, 1941. (*b*) Brown, W. E., and Sage, E. C.: Cardiac Disease Complicated by Pregnancy, Nebraska State M. J. **27**: 91, 1942.

5. The classification of the New York Heart Association was used:
   Class 1: Patients with cardiac disease and no limitation of physical activity.
   Class 2 (formerly 2*a*): Patients with cardiac disease and slight limitation of physical activity.
   Class 3 (formerly 2*b*): Patients with cardiac disease and decided limitation of physical activity.
   Class 4: Patients with cardiac disease who are unable to carry on any physical activity without discomfort.

6. Mendelson, C. L.: Management of Delivery in Pregnancy Complicated by Serious Rheumatic Heart Disease, Am. J. Obst. & Gynec. **48**: 329, 1944.

7. Jensen, J.: The Heart in Pregnancy, St. Louis, The C. V. Mosby Company, 1938.

8. (*a*) Allen, E., and Bauer, C. P.: Influence of Medical Disease on Obstetrical and Fetal Mortality, Am. J. Obst. & Gynec. **31**: 885, 1936. Consoli, D.: Note cliniche sulle cardiopatie complicanti lo stato puerperale, Clin. ostet. **39**: 249, 1937. Easby, M. H.: Early Recognition of Cardiac Insufficiency in the Presence of Pregnancy, M. Clin. North America **21**: 1059, 1937. (*b*) Enbring, G., and Sutton, D. C.: Heart Disease and Pregnancy, Illinois M. J. **72**: 147, 1937. (*c*) Lovibond, J. L.: Effects of Pregnancy on Certain Pre-Existing Diseases, Middlesex Hosp. J. **38**: 153, 1938. Maurizio, E.: Sulle cardiopatie in gravidanza, Atti soc. ital. di ostet. e ginec. **32**: 366, 1936. Schulze, M.: Study of Cardiac Disease Complicating Pregnancy, West. J. Surg. **44**: 80, 1936. Sferra, P.: Rendiconto statistico sopra 36 casi di cardiopatia e gravidanza ricoverati nella maternita nel biennio 1937-1938, Ann. di ostet. e ginec. **61**: 1155, 1939. Siedentopf, H.: Die herzkranke Schwangere, Med. Klin. **34**: 1058, 1938. Turino, T. R., and Wallace, J. T.: Resume of Cardiac Disease in Pregnancy for a Five-Year Period, Am. J. Obst. & Gynec. **45**: 526, 1943. Lesse, S.: The Prognosis of the Cardiac Patient in Pregnancy, ibid. **56**: 477, 1948.

9. Hedley, O. F.: A Study of 4,653 Cases of Rheumatic Heart Disease, Rheumatic Fever, Sydenham's Chorea and Subacute Bacterial Endocarditis Involving 5,921 Admissions to Philadelphia Hospitals, from January 1, 1930 to December 31, 1934, Pub. Health Rep. **55**: 1707, 1940.

not consent to this procedure, left the hospital and did not report for postpartum care. She reappeared during the twenty-seventh week of her next (seventh) pregnancy and was then in a state of congestive cardiac failure. Immediate hospitalization was urged in vain. The next day she was admitted with pulmonary edema.

TABLE 2.—*Effect of Heart Failure on Infant Mortality: Percentage Distribution*

	Infants Delivered of Normal Mothers Oct. 1939 to Oct. 1943		Infants Delivered of Mothers with Heart Disease But Not Having Heart Failure Oct. 1939 to Oct. 1948		Infants Delivered of Mothers with Heart Failure Oct. 1939 to Oct. 1948	
	No.	%	No.	%	No.	%
Total number of infants delivered	6,263	100	169	100	40	100
Born at term alive and well	5,452	87	149	88	28	70
Premature births alive and well*	392	6	9	5	6	15
Stillbirths, viable	129	2	4	2	2	5
Stillbirth, nonviable†	174	3	5	3	2	5
Neonatal deaths‡	116	2	2	1	2	5

* Infants whose birth weight was 5 pounds (2,268 Gm.) or less were considered premature.

† Infants weighing less than 3 pounds (1,361 Gm.) were classified as nonviable.

‡ Neonatal deaths included babies who died within forty-eight hours after birth.

After several days of intensive treatment her condition improved. She was advised to remain in the hospital until term, but she refused to do so. Several weeks later the physician who had attended her at home reported that she died undelivered. The third patient was a multiparous woman aged 38 whose condition was diagnosed as enlargement of the heart, mitral insufficiency, mitral stenosis, aortic insufficiency, questionable aortic stenosis and auricular fibrillation. In her first pregnancy, at the age of 23, she was given digitalis for a brief period. From 29 to 38 years of age she had had at least four attacks of heart failure. She was seen by us in the third month of her third pregnancy. Signs of congestive heart failure were noted,

TABLE 3.—*Effect of Advancing Pregnancy on Heart Failure*

Wks. of Gestation	No. of Patients Having Heart Failure*
1 to 4	0
5 to 8	0
9 to 12	2
13 to 16	0
17 to 20	4
21 to 24	4
25 to 28	4
29 to 32	4
33 to 36	7
37 to 40	7
Post partum	2

The expected date of delivery was taken as the end of fortieth week of gestation.

* Two patients whose onset of heart failure could not be dated are not included in this table.

and the customary therapy was instituted. She delivered spontaneously a premature child, who did well. A psychosis developed during the puerperium. Thirteen days later the family transferred the patient from the psychiatric medical service of Bellevue Hospital, against advice, to a private psychiatric institution in another city. The patient remained agitated and paranoid; she died 37 days post partum.

Infant Mortality.—The infants delivered on the obstetric service of Bellevue Hospital during the period of our study were classified for the purpose of this analysis into three groups: infants of mothers with normal hearts, infants of mothers with rheumatic heart disease without failure and infants of mothers with rheumatic heart disease with failure (table 2 and fig. 1). The mortality rate for infants of mothers with compensated heart disease was not significantly higher than for infants of normal mothers. The mortality rate for infants of mothers with congestive heart failure was 15 per cent, whereas in the compensated group it was 6 per cent and in those with normal hearts 7 per cent.

Congestive Heart Failure.—In 36 of the 205 patients congestive cardiac failure developed during pregnancy, an incidence of 17.6 per cent.[10] Failure occurred most frequently during the second half of pregnancy (table 3). Contrary to other reports, no decline in the incidence of failure was observed in the last lunar month.

The interval of time from the onset of the first rheumatic manifestation to the observed pregnancy was determined in 145 patients (table 4, fig. 2).[11] As the interval lengthened, the incidence of cardiac failure increased. Of those who had had rheumatic fever for less than ten years, 4 per cent went into cardiac failure during pregnancy; but of those who had had it longer than twenty years, 37 per cent became decompensated.

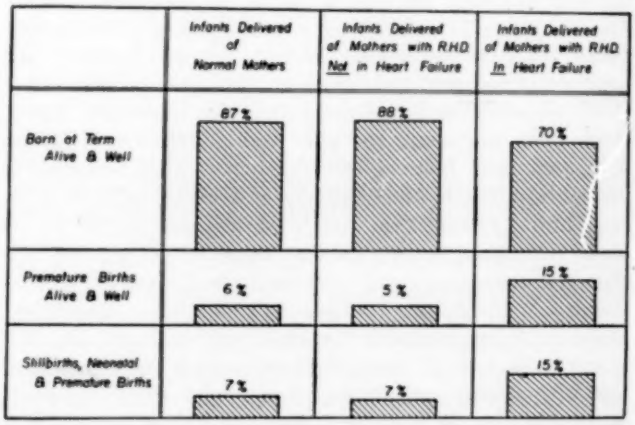

Fig. 1.—Effect of maternal heart failure during pregnancy on infant mortality.

Patients whose cardiac reserve failed had had heart disease for an average duration of eighteen years, five years longer than those in whom it did not fail.

The average age of the group in cardiac failure was 29.3 years, but the average age of the group without failure was 24.6 years (table 5, fig. 3).

A close relationship was observed between the limits of cardiac reserve that existed before pregnancy and the incidence of failure during pregnancy. Only 4 of the 118 patients in classes 1 and 2[5] had congestive heart failure, whereas 32 of the 87 patients in classes 3 and 4 presented this complication (table 6).

A history of previous cardiac failure was likewise found to be significant. In 89 per cent of those patients whose hearts decompensated during a previous pregnancy they did so again during the observed pregnancy. In only 12 per cent of those who had never had heart failure before did it develop during the observed pregnancy (table 7).

It has been stated that when the aortic valve is damaged the patient faces a greater risk during preg-

10. The criteria for congestive cardiac failure were pulmonary edema, paroxysmal nocturnal dyspnea, basal rales or a palpable, tender liver.

11. In the other cases either there was no initial episode or the patient did not remember it.

nancy than when the mitral valve alone is involved.[12] Our experience does not confirm this observation. Table 8 shows that failure was more common in patients with mitral stenosis (24 per cent) than it was in those who had aortic or combined aortic and mitral valvular disease (16 per cent).

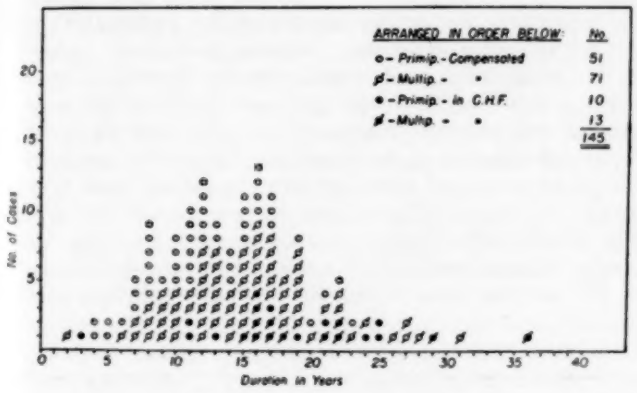

Fig. 2.—Rheumatic heart disease in pregnancy. Graphic representation of 145 cases with known duration of rheumatic heart disease.

The size of the heart was determined by teleroentgenograms at several intervals during and after pregnancy in 49 patients who did not have cardiac failure and in 10 who did. The maximum transverse diameter of the heart was measured and the percentage of enlargement was calculated according to the table of Ungerleider and Clark.[13] The weight of the patient at the time the radiogram was made was used uncorrected when making the calculations. The results during pregnancy approximated postpartum cardiac measurements within a range of 10 per cent or less. Cardiac measurement by such a method therefore seems reliable, even though the configuration and position of the heart changes as gestation advances. None of the patients whose hearts were enlarged less than 10 per cent above normal had cardiac failure. Contrariwise, all patients who had cardiac failure showed an increase of

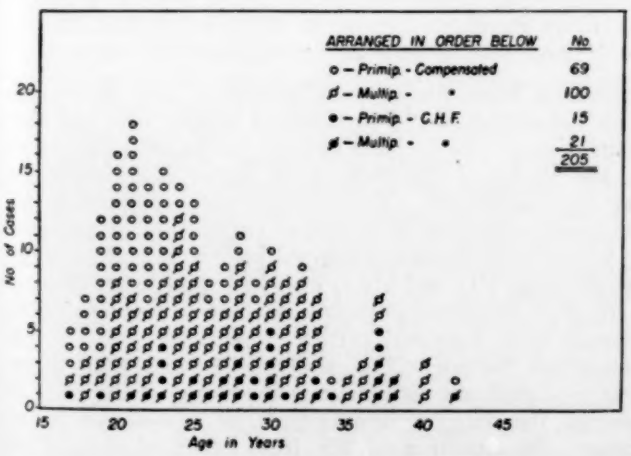

Fig. 3.—Rheumatic heart disease in pregnancy. Graphic representation of 205 cases arranged according to age.

10 per cent or more above normal heart size. However, a number of women with 20 to 30 per cent enlargement did not experience cardiac decompensation. It was concluded from this that, although patients with minimal cardiac enlargement are better risks, those with moderate enlargement are not necessarily bad risks. As far as these limited observations indicated, there was a general but not a strict correlation between the degree of enlargement and the likelihood of failure of the heart.

The prognosis in all patients with rheumatic heart disease, men and women, has been found to be more favorable when the original manifestations consisted of chorea or pains of muscles and joints rather than polyarthritis or carditis.[14] We have found this to be true also for pregnant patients with cardiac disease. Only 1 of the 43 patients who had had chorea or muscular and articular pains as the sole rheumatic manifestation had cardiac failure during the observed pregnancy. Ten of the 60 patients who had had polyarthritis alone and 6 of 10 patients who had had both polyarthritis and chorea manifested decompensation of

TABLE 4.—*Effect of Duration of Disease on Heart Failure*

Duration in Years	Total Patients in Group	Patients Not Having Heart Failure	Patients with Heart Failure	Per Cent Patients with Heart Failure
0 to 9	25	24	1	4.0
10 to 14	46	42	4	8.7
15 to 19	50	42	8	16.0
20 and over	24	15	9	37.5
Duration unknown*	60	46	14	23.3
Average duration		13.0 yr.	18.7 yr.	

* Patients who did not know they had heart disease until coming to clinic or who were without a history of previous rheumatic manifestations.

TABLE 5.—*Effect of Age on Heart Failure*

Age Groups in Years	Total	Patients Not Having Heart Failure	Patients with Heart Failure	Per Cent Patients with Heart Failure
Under 20	24	22	2	8.3
20 to 24	77	71	6	7.8
25 to 29	49	38	11	22.5
30 to 34	36	27	9	25.0
35 and over	19	11	8	42.1
Average age	..	24.6 yr.	29.3 yr.	....

the heart. The difference between the first and second group and that between the second and third group have been subjected to statistical analysis and found to be significant. Evidently polyarthritis or a combination of polyarthritis and chorea implies severer infection and consequently greater cardiac damage than chorea alone.

There was no difference in the rate of failure of the heart among primiparous as compared with multiparous women (table 9).

COMMENT

The natural history of rheumatic heart disease may be said to consist of four phases: (1) an initial infection, which may be manifested by carditis, polyarthritis, chorea or pains of muscles and joints; (2) one or more recrudescences, which, like the primary episode, may follow a hemolytic streptococcic infection; (3) an inactive period, lasting usually from puberty or adolescence to the fourth decade, in which there are usually neither recurrences nor evidence of decreasing functional capacity, and (4) a diminution in cardiac reserve, lead-

12. (*a*) Naish, F. C.: Study of Immediate and Remote Effects of Pregnancy on Heart Disease, J. Obst. & Gynaec. Brit. Emp. **44**: 659, 1937. (*b*) Corwin, J.; Herrick, W. W.; Valentine, M., and Wilson, J. M.: Pregnancy and Heart Disease, Am. J. Obst. & Gynec. **13**: 617, 1927. Jensen.[7]

13. Ungerleider, H. E., and Clark, C. P.: A Study of the Transverse Diameter of the Heart Silhouette with Prediction Table Based on the Teleroentgenogram, Am. Heart J. **17**: 92, 1939.

14. Kaiser, A. D.: Factors That Influence Rheumatic Disease in Children, J. A. M. A. **13**: 886 (Sept. 22) 1934. Ash, R.: Prognosis of Rheumatic Infection in Childhood, Am. J. Dis. Child. **52**: 280 (Aug.) 1936. Jones, T. D.: Heart Disease in Childhood, Am. J. Pub. Health **28**: 637, 1938. Lichtwitz, L.: Pathology and Therapy of Rheumatic Fever, New York, Grune & Stratton, Inc., 1944.

ing progressively to congestive heart failure and later death. When auricular fibrillation supervenes, it usually occurs during the last phase and is essentially a reflection of the long duration of the disease. Phase 3, the period when the heart disease is inactive, is the one during which pregnancy usually occurs: this explains why the majority of patients do well when under intelligent obstetric care. It is of utmost importance to recognize when a woman who is pregnant or contemplating pregnancy is approaching phase 4. Cardiac failure ranks first among the causes of maternal deaths in patients with heart disease and is the only cause amenable to therapy, especially when detected early.

TABLE 6.—*Effect of Functional Capacity on Heart Failure*

Functional Classification*	Total Patients	Patients Not Having Heart Failure	Patients with Heart Failure	Per Cent Patients with Heart Failure
Class 1	52	51	1	1.9
Class 2	66	63	3	4.5
Class 3	83	55	28	33.7
Class 4	4	0	4	100.0
Total	205	169	36	17.6

* Classification of the New York Heart Association.[5]

How long a given patient is likely to remain in phase 3 before entering phase 4 will depend, in the main, on the age at onset of initial manifestation, the number of years that have elapsed since this infection, the severity and nature of the infection (carditis is more serious than polyarthritis and the latter is severer than chorea) and the frequency and number of recurrences. When there is no previous history of any rheumatic manifestation by which to determine the duration of the disease, the absolute age of the patient may be used as a rough index.

Complications such as subacute bacterial endocarditis, embolization and intercurrent infections may occur in any phase and may seriously alter the course of events as here outlined.

Effect of Pregnancy on Duration of Life.—The question whether pregnancy alters the course of rheumatic heart disease or shortens the life of the patient is of fundamental importance. In several groups the reported age of death was younger in nulliparous than in parous women.[7] When the sample was reduced to include only those who lived to a "marriageable age," the same results were obtained.[15] Furthermore, when only those who died of congestive heart failure were considered and the group was subdivided into those who survived past the age of 18 years and those who survived past the age of 40 years, there was no significant difference in the average age at death between nulliparous and parous women.[15a] In this last group those who died during pregnacy were not included.

TABLE 7.—*Correlation Between Previous Heart Failure and Failure in Observed Pregnancy*

	Total	No. of Patients Who Did Not Have Heart Failure in Observed Pregnancy	No. of Patients Who Had Heart Failure in Observed Pregnancy	Per Cent Patients Who Had Heart Failure in Observed Pregnancy
Patients who had heart failure previously	20	7*	13	65.0
Patients who did not have heart failure in the past	185	162	23	12.4
Total	205	169	36	17.6

* Five of these 7 patients had heart failure during an acute attack of rheumatic carditis and not during pregnancy.

The reports quoted in the foregoing paragraph are subject to some criticism. Several important factors in the nulliparous and parous groups were not controlled; these include age at onset of heart disease, number and severity of recurrences of rheumatic fever, functional capacity of the heart and the respective duration from onset of heart disease to failure and from failure to death. These factors were carefully considered and controlled in an analysis made by Cohn and Lingg,[16] who compared the clinical course and life span of 169 women who bore one or more children after rheumatic heart disease was known to have developed with the course of 215 nulliparous women who had the same disease. All patients in both groups were observed in the clinics of the New York Heart Association to the time of death. The groups were comparable in that each consisted of a similar proportion of patients in whom heart disease developed before the childbearing period (age 19) and after, who had mild heart disease with good functional capacity and who had severe heart disease with impaired cardiac reserve or episodes of congestive failure. The analysis showed that there was no significant difference in the tempo of the clinical course, the rate of development of congestive heart failure, the duration of life from onset of disease to death and the age at death in the parous and the nulliparous groups.

TABLE 8.—*Effect of Valvular Lesions on Heart Failure*

Valvular Lesions	Patients Not Having Heart Failure	Patients with Heart Failure	Per Cent Patients with Heart Failure
Mitral insufficiency with enlarged heart	44	2	4.4
Mitral stenosis and mitral insufficiency	82	26	24.1
Aortic insufficiency alone or with other valvular lesions	43	8	15.7
Total	169	36	17.6

TABLE 9.—*Effect of Parity on Heart Failure*

Age Group in Yrs.	Primpara		Multipara	
	Patients Not Having Heart Failure	Patients with Heart Failure	Patients Not Having Heart Failure	Patients with Heart Failure
Under 20	16	2	6	0
20 to 29	52	6	58	10
30 to 39	3	7	30	10
40 and over	0	0	4	1
Total	71	15	98	21
Percentage of patients with heart failure	..	17	..	17

This reassuring conclusion applies only to those who survive the period of gestation. Pregnacy entails certain risks for the patient with rheumatic heart disease which one who is not pregnant obviously does not face. Failure or death which may occur during or soon after pregnancy might not have resulted had the patient not become pregnant. Assuming, however, that

15. (*a*) Boyer, N. H., and Nadas, A. S.: The Ultimate Effect of Pregnancy on Rheumatic Heart Disease, Ann. Int. Med. **20**: 99, 1944. (*b*) Enbring and Sutton.[5b]

16. Cohn, A. E., and Lingg, C.: Unpublished data.

the patient does survive the pregnancy, the subsequent course of the disease will probably remain unaltered.

Age: Patients with rheumatic cardiac disease, regardless of parity, are more prone to fail as they get older. Patients above the age of 35 years (table 5) are much more apt to have cardiac decompensation than those who are younger.

Duration: If the time of onset of heart disease were known, then the duration from onset to pregnancy would undoubtedly be more dependable as a prognostic guide than the absolute age of the patient. Lacking this precise information in all cases, we have arbitrarily taken the first rheumatic manifestations as the time of onset. This does not imply that the heart disease necessarily begins at this time. As has been mentioned, there is a closer correlation between duration of disease and cardiac failure than between absolute age and failure.

Enlarged Heart: That the heart actually increases in weight during pregnancy has not yet been clearly demonstrated. In women with similar rheumatic valvular lesions who died of congestive cardiac failure, the heart was found to be of approximately the same weight at autopsy regardless of whether the patients had no, few or many pregnancies.[15a] Thus, it is likely that pregnancy causes no permanent cardiac enlargement. Since the heart increases in size as the duration and severity of the disease increases, the risk of cardiac failure is naturally greater in pregnant women whose hearts are decidedly enlarged.[17] Yet we have found that heart size is not as significant an index of prognosis as other factors here considered.

Valvular Lesions: There is no unanimity of opinion as to the seriousness of the combination of mitral stenosis and aortic insufficiency as compared with mitral stenosis alone. Some observers attach grave significance to the coexistence of mitral and aortic lesions,[12] but others state that there is no significant difference between the two groups.[18] Our experience corresponds with that of those who attribute no greater gravity to combined aortic and mitral valvulitis than to mitral stenosis alone. Data collected by us from reports published since 1936 show no significant difference between the mortality rates among pregnant women with combined mitral and aortic valvulitis and those with mitral valvulitis alone (table 10).

Functional Class and Previous Failure: The functional capacity of the heart to do work is without doubt the most reliable single index of the prognosis in pregnancy. At times, however, it is difficult to establish this with precision, and it may vary from one month of pregnancy to another. An actual test of pregnancy is therefore more reliable; hence, it is evident that a patient who had had failure of the heart in a previous pregnancy will almost certainly have decompensation again unless the cardiac failure was due to circumstances not likely to recur, such as active rheumatic carditis.[19] It is not true that patients who have not had cardiac failure previously will not have it in a later pregnancy. In our series in 12 per cent of the multiparous patients who had no history of cardiac failure there was decompensation during the observed pregnancy.

Multiparity: Conflicting opinions have been expressed on parity: such as, the prognosis is worse in primiparas [17d]; it is worse in multiparas,[20] and parity has no important bearing on the prognosis.[21] This discrepancy may have resulted from the fact that the different authors did not control, at least to the same degree, two factors that influence the outcome, namely, the duration of heart disease (longer in multiparas) and the physical effort spent in obstetric labor (greater in primiparas). From the results in this series (table 9) it is clear that parity has no real significance.

A number of factors should be considered in evaluation of the prognosis of pregnancy in patients with heart disease. Some of these are more important than others,

TABLE 10.—*Deaths Among Pregnant Rheumatic Cardiac Patients Grouped According to Valvular Lesions (1936 to 1948)*

	Mitral Valvulitis Alone			Aortic or Aortic and Mitral Valvulitis Combined*		
	Patients	Deaths		Patients	Deaths	
	No.	No.	%	No.	No.	%
Harris, K.: Lancet **1**: 677, 1937	81	6	7.4	19	2	9.5
Lamb,[17a] 1937	89	5	5.6	12	2	16.7
Naish,[12a] 1937	349	10	2.9	78	2	3.9
Hay, J.: Post-Grad. M. J. **12**: 143, 1939	56	1	1.8	10	0	0
Bramwell, C., and Longson, E. A.: Heart Disease and Pregnancy, in Bramwell, C., and King, J. T.: Principles and Practice of Cardiology, London, Oxford University Press, 1942, pp. 216-230	260	20	7.7	31	1	3.2
Jensen, J.; Wegner, C.; Keys, E. H., and Smith, H. R.: Am. J. Obst. & Gynec. **39**: 443, 1940	88	6	6.8	11	1	9.1
Hamilton and Thomson,[4a] 1941	581	28	4.7	148	8	5.3
Stromme, W. B., and Kuder, K.: Am. J. Obst. & Gynec. **52**: 264, 1946	565	7	1.2	90	1	1.1
Evans, P. R. C.: Guy's Hosp. Rep. **96**: 194, 1947	72	4	5.5	13	4	30.7
Bunim and Appel	154	1	0.7	51	2	3.9
Total	2,295	88	3.8	463	23	4.9

* Forty-nine of these 463 patients had aortic valvulitis alone, 414 had combined mitral and aortic valvulitis.

but each of them fits into a more inclusive principle, which is based on the orientation of the patient in the natural course of her heart disease. The validity of applying this principle to pregnant cardiac patients is supported by the evidence that gestation does not alter the course of the disease.

SUMMARY

In determining the prognosis in pregnancy of 216 women with rheumatic heart disease, we considered the following factors: duration of rheumatic fever, age, functional capacity, history of previous failure, type of valvular damage, size of heart, nature of earlier rheumatic manifestations and parity. It was found that the important signs were those which helped prognosticate congestive failure of the heart. That cardiac failure is the governing feature in prognosis is supported by the observation that it is the most common cause of death in pregnancy complicated by rheumatic heart disease.

The factors found to be important in prognosticating cardiac failure and in estimating the risk involved in

17. (*a*) Lamb, A. E.: Heart Disease in Pregnancy, Am. J. Obst. & Gynec. **34**: 456, 1937. (*b*) Pardee, H. E. B.: Experiences in the Management of Pregnancy Complicated by Heart Disease, ibid **17**: 255, 1929. (*c*) McIlroy, L., and Rendel, O.: The Problem of the Damaged Heart in Obstetrical Practice, J. Obst. & Gynaec. Brit. Emp. **38**: 7, 1931. (*d*) Bramwell, C.: Prognosis of Heart Disease in Pregnancy, Lancet **1**: 629, 1935.

18. Hamilton, B. E.: Sixteen Years' Experience with Heart Disease in Pregnant Women, Am. Heart J. **14**: 555, 1937. McIlroy and Rendel.[17c]

19. (*a*) Gorenberg, H., and McGleary, J.: Rheumatic Heart Disease in Pregnancy, Am. J. Obst. & Gynec. **41**: 44, 1941. (*b*) Hamilton, B. E., and Kellogg, F. S.: Cardiac Disease in Pregnancy, J. A. M. A. **91**: 1942 (Dec. 22) 1928. Hay, J., and Hunt, E.: Pregnancy and Parturition in Patients with Crippled Hearts, Lancet **1**: 271, 1928. (*c*) Sheehan, H. L., and Sutherland, A. M.: Pathology of Heart Disease in Pregnancy, J. Obst. & Gynaec. Brit. Emp. **47**: 597, 1940. (*d*) Carr, F. B.: Heart Disease in Pregnancy, M. Ann. District Columbia **10**: 16, 1941.

20. Gilchrist, A. R., and Murray-Lyon, R. M.: Does Pregnancy Hasten the Fatal Termination in Rheumatic Heart Disease, Edinburgh M. J. **40**: 587, 1933. Naish.[12a]

21. Oppel, T. W.: Congestive Heart Failure in Pregnancy, Am. J. Obst. & Gynec. **39**: 24, 1940. Sheehan and Sutherland.[19c]

pregnancy form integral parts of a basic principle, which consists of establishing the patient's position in the natural course of her rheumatic heart disease. This principle gains validity when data collected under well controlled conditions indicate that pregnancy per se does not alter the course of this disease. The application of this principle for determining prognosis led to interruption (per vagina) of only 11 of 216 pregnancies. No hysterotomies were performed after the patient was permitted to pass through the first trimester of pregnancy. There were no deaths from congestive heart failure among the 202 patients who remained under our care through pregnancy and parturition.

477 First Avenue (16) (Dr. Bunim).

ABSTRACT OF DISCUSSION

Dr. Julius Jensen, St. Louis: The authors contend that the time in the course of the rheumatic disease at which pregnancy occurs constitutes a valuable prognostic criterion. That would be true if it were known that rheumatic heart disease had a predestined, time-limited course. It is not known why patients with rheumatic heart disease eventually have congestive failure. The evidence is inconclusive whether the disease has a time-limited course ending in heart failure, whether heart failure occurs because of some intercurrent (rheumatic?) infection or whether degenerative changes added to the damage caused by the original infection prove too much for the heart. The first explanation is least likely, because the survival period from the original attack of rheumatic fever varies so greatly; 5 to 8 per cent of the patients survive to old age. If heart failure is caused by some intercurrent infection, the end of rheumatic heart disease would be fortuitous. If degenerative changes cause heart failure, physiologic age rather than survival period since the original infection would be the determinant. Therefore, the final acceptance of the thesis that the prognosis of heart disease and pregnancy depends on the period of survival since the original infection rather than on the age of the patient must await a better understanding of the cause or causes of heart failure in rheumatic heart disease. The authors state that they have reduced interruptions of pregnancy to 11 in 200 pregnancies. This would appear rather high by modern standards unless the series is loaded with patients having severe heart disease. It is the ultimate purpose in this work to obtain a live mother and a healthy baby, and this can be obtained only by having available for study full details of as many cases as possible in which interruption of pregnancy was performed. In this series no patient died while receiving adequate antepartum care. Mortality statistics of this kind may be divided into cases in which adequate antepartum care was given and those in which the patient failed to receive such care. Such a division would emphasize the therapeutic advances in the field. The authors state that the presence of rheumatic heart disease is, in itself, no longer a cause for cesarean section. Whether it should be entirely abandoned must be finally determined when physicians fully understand the effects of surgical operation and of obstetric labor on the human organism. The fact that after surgical operations the adrenal cortex is largely depleted of cholesterol and ascorbic acid suggests some profound effect which is, as yet, not understood.

Dr. Burton E. Hamilton, Boston: It is reassuring that Dr. Bunim and Dr. Jensen and I agree. I have no adverse criticism of the case analyses just presented. Women with chronic rheumatic heart disease who have had children live as long as those who have not. The inference that pregnancy is therefore good for rheumatic heart disease is incorrect. It is the cardiac persons in better health who marry and become pregnant. Pregnancy increases the work of the heart materially —cardiac persons not severely handicapped have a slightly greater risk of death than in a year of ordinary living; the severely handicapped patients, a 2 or 2½ times greater risk; those with auricular fibrillation, a 4 times greater risk. The prognostic importance of estimating when a patient with rheumatic heart disease in the third (quiescent) stage is approaching the fourth stage has been emphasized. I would emphasize that downhill progress is neither uniform nor inevitable. Of the many factors in prognosis, some are controllable. In Boston Lying-in Hospital maternal mortality for women with rheumatic heart disease fell critically from 15 to 20 per cent to 3 to 4 per cent after the heart clinic was developed. The critical drop occurred in 1923. Subsequent improvement in maternal mortality was hardly perceptible until the last six years. With the cardiac persons divided into favorable and unfavorable groups, the latter had as high a death rate from 1935 to 1945 as they did from 1921 to 1934. Pregnancy cannot be made safe for the crippled cardiac persons. The proportion of cardiac persons in whom conditions were unfavorable for safe pregnancy has dropped from 30 to 10 per cent. Why? Cardiac children now grown to marriage and pregnancy were discovered and were treated by the physicians in fifteen cardiac clinics that have functioned in Boston for over twenty years. The cardiologists lowered mortality in rheumatic heart disease in obstetric hospitals. Now cardiac clinics provide cardiac patients in better physical condition for the obstetric clinics. The next advance must be made by students of pregnancy. Maternal mortality has improved faster in general than for the patients with cardiac conditions, so that at the Boston Lying-in the percentage of all maternal deaths furnished by the patients with rheumatic heart disease has doubled. The obstetricians must be interested. Cardiac persons who are poor childbearing risks and who die are fewer, but some will appear as long as the disease exists. Can normal pregnancy be made easier for them? It is normal in pregnancy to have increased circulating blood volume, retention of fluid and blood dilution, but it is not desirable for the heart. Profound changes in circulation occur when the uterus is emptied.

Dr. Nicholson J. Eastman, Baltimore: Every gravida with rheumatic heart disease has her best interest served only by close cooperation between the cardiologist and the obstetrician. Diagnosis is often difficult. Prognosis is precarious in many instances, and in these matters and others obstetricians are dependent in large measure on the advice of their cardiologic confreres. The prognosis is usually good in these women. Dr. Bunim's figures show that in his 256 cases only 11 therapeutic abortions were deemed necessary, or 4.8 per cent. Experience with therapeutic abortion at the Johns Hopkins Hospital in cases of rheumatic heart disease over the past four years shows that in 466 cases the incidence of therapeutic abortion is higher than Dr. Bunim's, namely, 9.4 per cent. It will also be observed that during the last six of these twelve years the rate has been reduced to 6.2 in the last 205 cases. This rate of 6.2 per cent is in close agreement with Dr. Bunim's 4.7 per cent. Throughout the country too many therapeutic abortions are being performed for rheumatic heart disease in pregnancy, and it is worth while to emphasize that among these patients not more than 1 in 20 calls for interruption of pregnancy. Although therapeutic abortion is not often required in rheumatic heart disease, when it is indicated it is urgently indicated, as in cases in which there is a history of previous heart failure. This statement is well documented by Dr. Bunim's statistics, which show that in patients who had heart failure in their previous pregnancy, 89 per cent had repeated heart failure in pregnancy. Among patients who had had any kind of heart failure previous to gestation, 65 per cent had repeated heart failure in the course of pregnancy. This risk is too much to impose on mothers, at least as I assess life's values. I should like to reaffirm Dr. Bunim's statement that cesarean section is never indicated because of rheumatic disease. All cardiologists know this; all obstetricians know this, yet the country over many unnecessary cesarean sections are done because of rheumatic heart disease to the detriment of these patients.

Dr. Joseph J. Bunim, New York: I should like to emphasize one point made by Dr. Eastman, namely, the importance of cooperation between the obstetrician and cardiologist. This statement has appeared many times in the literature, yet it would be well to support it with some pertinent facts and figures. Most of the series reported in the literature show an average mortality rate of 3.4 per cent. But in almost every series there has been careful and close collaboration between the

obstetrician and internist. Where there has not been such collaboration, there usually has been no published report. Dr. Hedley of the U. S. Public Health Service analyzed the records of such patients in the hospitals in Philadelphia, where there were no special prenatal cardiac clinics. He found that for pregnant women with rheumatic disease admitted to these hospitals in the year 1934, the mortality rate was 18 per cent. This is six times as high as that reported from special clinics where obstetricians and internists worked together. Dr. Jensen has raised the question of the effect of pregnancy on the life span of patients with other types of heart disease. It may be true that there is a deleterious or unfavorable effect of pregnancy on patients who have preeclampsia or hypertensive heart disease. We do not have data on that type, but as far as rheumatic heart disease is concerned, we believe that, provided the patient goes through pregnancy successfully, having been pregnant will not alter the course of her disease or shorten her life. When a patient with heart disease becomes pregnant, she undertakes risks which a woman who does not become pregnant avoids. However, if she does not have any difficulty during the pregnancy, particularly if congestive heart failure does not develop, and if she survives the pregnancy, then the rest of her course as a cardiac patient will remain unaltered and her life will not have been shortened by one, two or more pregnancies.

AQUEOUS PROCAINE PENICILLIN

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Chicago

This study is presented to demonstrate that sustained therapeutic levels of penicillin can be attained by relatively infrequent injections of an aqueous solution of procaine penicillin. The method used reduced the disadvantage of rapid excretion seen following injection of aqueous penicillin and the unfavorable side reactions due to vehicles such as oil or wax used in other long-acting penicillin preparations. Experience has shown that a large variety of bacteria are susceptible in vitro to concentrations of penicillin ranging between 0.04 and 0.2 units per cubic centimeter. Other organisms such as certain alpha and gamma streptococci require greater amounts for in vitro inhibition. The optimum in vivo penicillin level appears to be 2 to 20 times the in vitro inhibitory level. This optimum level occupies a narrow range, above or below which bacterial death seems to go on at a relatively slower rate. Therefore, in dealing with many of the usual bacterial infections, a penicillin concentration of 0.1 to 1 unit per cubic centimeter would be optimum.[1] Higher concentrations are indicated in specific infections in which the individual in vitro sensitivity is above the usual level.

Blood plasma or serum penicillin levels offer a convenient gage of penicillin absorption, excretion and tissue-plasma diffusion. If a certain continuous tissue penicillin level is to be maintained, a corresponding plasma penicillin level must exist. Bacteria in tissue may be killed by the intermittent presence of penicillin, but if optimum concentration is lacking for too long a period, the time required for cure may be prolonged.[2]

Aqueous procaine penicillin is absorbed and excreted at a much slower rate than aqueous penicillin following a single injection, as shown by Whittlesey and Hewitt.[3] Serum penicillin levels ranging between 0.02 and 0.64 unit per cubic centimeter were demonstrated twelve hours after injection of 300,000 units aqueous procaine penicillin. Twelve hours after injection of 600,000 units of the drug, levels ranging between 0.04 and 1.28 units per cubic centimeter were demonstrated. This study is concerned chiefly with prolonged therapeutic levels of penicillin in the blood after multiple injections of aqueous procaine penicillin.

From the Rush Department of Medicine of the Presbyterian Hospital and the University of Illinois College of Medicine.

1. Eagle, H., and Musselman, A. D.: The Rate of Bactericidal Action of Penicillin as a Function of Its Concentration, and Its Parodoxically Reduced Activity at High Concentrations Against Certain Organisms, J. Exper. Med. **88**: 99 (July 1) 1948.

2. Eagle, H.: Speculations as to the Therapeutic Significance of the Penicillin Blood Level, Ann. Int. Med. **28**: 260 (Feb.) 1948.

3. Whittlesey, P., and Hewitt, W. L.: Serum Concentrations of Penicillin Following Administration of Crystalline Procaine Penicillin G in Aqueous Supsension, Proc. Soc. Exper. Biol. & Med. **68**: 658 (July-Aug.) 1948.

METHODS

Aqueous procaine penicillin[4] was administered to 54 patients in varying doses at twelve hour intervals. Blood was drawn for penicillin levels just prior to the next injection of penicillin, so that the minimum penicillin concentration could be determined. Penicillin levels were measured by the tube dilution method using Bacillus subtilis as a test organism. Over seven hundred determinations were made.

TABLE 1.—*Summary of Infections Treated with Aqueous Procaine Penicillin, Bacterial Sensitivity Determinations and Final Result*

	Result		Sensitivity Determinations
	Improved	Died	
Prophylactic postoperative	20	..	..
Streptococcic infections			
Alpha hemolytic, subacute bacterial endocarditis	4	2	6
Beta hemolytic, pharyngitis and erysipelas	2	..	1
Staphylococcic infections			
Osteomyelitis	3	..	3
Skin infections and cellulitis	5	..	..
Secondary infection in disseminated lupus erythematosis	1	..	..
Pneumococcic infections			
Lobar pneumonia	1	..	1
Bronchopneumonia (organisms not determined)	3	..	..
Gonococcic infection			
Salpingitis	1	..	..
Spirochetal infections			
Syphilis—early, late, latent and central nervous	5	..	..
Vincent's stomatitis	1	4	..
Virus infections			
Lymphogranuloma venereum	2	..	..

TABLE 2.—*Frequency of Penicillin Determinations*

Number of Determinations							
2 to 4	5 to 9	10 to 19	20 to 39	40 to 59	60 to 79	80 to 99	100
Number of Patients							
23	13	9	5	1	1	1	1

CLINICAL DATA

Table 1 indicates the various conditions treated and the ultimate result. Control of infection was satisfactory. Dosage was determined in many cases by the type of infecting organism and in 11 cases, including those of subacute bacterial endocarditis, on an in vitro sensitivity basis. In the usual infections and in the postoperative cases a fixed dose schedule of 200,000 or 300,000 units twice a day was used. Penicillin in amounts up to 10,000,000 units twice a day was given. The number of determinations made on each patient varied from two to over one hundred. Table 2 shows the frequency of penicillin determinations.

DOSAGE AND BLOOD LEVELS

Figure 1 is a summary of the sustained minimum penicillin blood levels determined twelve hours after injection of aqueous procaine penicillin. Observations

4. Supplied by E. R. Squibb & Sons as penicillin procaine G, for aqueous injection.

are combined according to similar doses of penicillin. Variation in blood levels is represented by bars plotted in percentages of the total number of determinations. The larger doses were used in cases of subacute bacterial endocarditis in which, with 1 exception, the in vitro sensitivity of the streptococcus ranged between

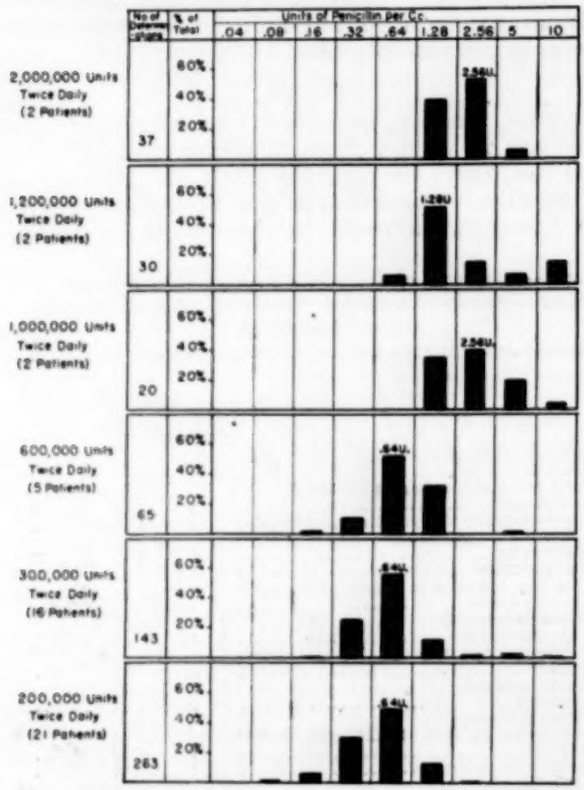

Fig. 1.—Sustained minimum penicillin blood levels determined twelve hours after injection of aqueous procaine penicillin.

0.04 and 0.08 unit of penicillin per cubic centimeter. It is evident that doses of 1,000,000 to 2,000,000 units of aqueous procaine penicillin injected twice daily gave sustained blood levels ranging between 0.64 and 10 units per cubic centimeter. This represents a concentration of at least 10 to 20 times the in vitro sensitivity of the organism, and in frequent instances many times more. This dosage may be somewhat excessive but was used to attain optimum minimum blood levels.

Dosages of 200,000 and 300,000 units of the drug administered twice daily were employed most frequently in a total of 37 patients with four hundred and six twelve-hour determinations. About one half of these determinations measured 0.64 unit per cubic centimeter with a significant range between 0.16 and 1.28 units. Injection of 600,000 units of penicillin twice daily gave slightly higher blood levels. This range of 0.16 to 1.28 units per cubic centimeter is comparable to the recommended level of 0.1 to 1 unit suggested by Eagle as the result of extensive bacteriologic study. The clinical response to therapy of infection was satisfactory. The patients who died were in the terminal stages of carcinoma.

INITIAL RISE IN LEVEL OF PENICILLIN

The initial rise of the level of penicillin in the blood stream was also determined in 8 patients. A prompt rise in three hours occurred with sustained levels at twelve hours. A high peak at three hours comparable to that obtained with aqueous penicillin was not observed.

RENAL INSUFFICIENCY

The factor of renal insufficiency and also of dehydration materially elevated the anticipated sustained blood levels. In a number of patients with chronic renal insufficiency and nitrogen retention, penicillin blood levels as high as 20 units per cubic centimeters were observed on a dosage of 300,000 units twice a day. This factor also delayed excretion of penicillin when therapy was discontinued; as long as 8 days later 0.02 unit of penicillin per cubic centimeter was detectable.

DURATION OF EXCRETION

The terminal excretion of penicillin was observed in 8 patients for a period of four days. The dosage given these patients ranged between 200,000 and 1,000,000 units twice a day. At the end of forty-eight hours, blood levels between 0.08 and 0.64 unit per cubic centimeter were observed, the higher levels corresponding to the greater dosage. At ninety-six hours penicillin could be detected in those patients who received larger amounts. Retention of penicillin concerns the evaluation of clinical signs of cure. That is, penicillin therapy ceases not on the day when the last injection is given but two to four days later.

PENICILLIN RESISTANCE

The problem of therapy in a case of subacute bacterial endocarditis due to a penicillin-resistant streptococcus, with the use of 10,000,000 units of penicillin for two months, is of special interest. The patient previously had been treated with other penicillin preparations. The alpha streptococcus causing the infection required 6 units of penicillin per cubic centimeter for inhibition in vitro. Penicillin blood levels are shown in figure 2. Phase I of figure 2 shows blood levels of

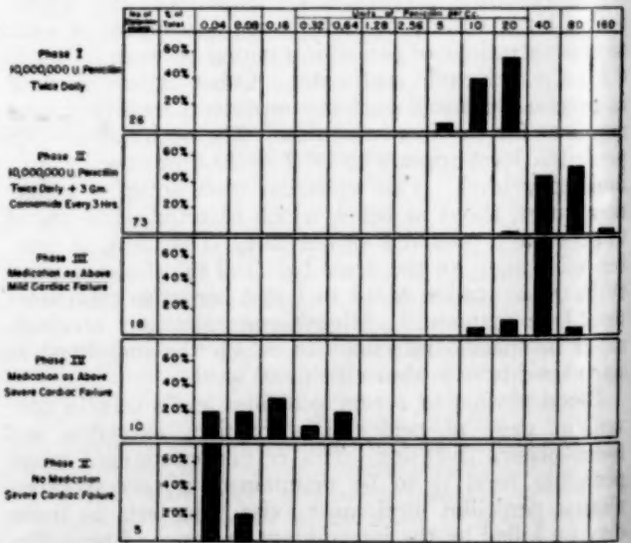

Fig. 2.—Sustained minimum penicillin blood levels determined twelve hours after injection of aqueous procaine penicillin in a case of subacute bacterial endocarditis.

20 units per cubic centimeter during the initial phase of therapy. After the addition of carinamide the blood levels rose to 40 to 160 units per cubic centimeter and fluctuated at these levels for five weeks. Blood cultures were sterile. Phase III shows the decline in penicillin blood levels due to mild cardiac failure. Phase IV demonstrates a precipitous drop in blood levels from 20 to 0.64 unit per cubic centimeter which occurred with acute cardiac decompensation. At the time of severe cardiac failure the penicillin pooled in the tissues

at the site of injection. Phase V shows the terminal penicillin levels of 0.04 to 0.08 unit per cubic centimeter after penicillin therapy was discontinued. Autopsy on this patient showed ruptured chorda tendinae and healing vegetations on the mitral valve. Bacteria were not seen in the stained microscopic section. The patient tolerated exceedingly well for two months the injection twice daily of over 30 cc. (10,000,000 units) of penicillin.

REACTIONS

In this series of patients the undesirable side reactions of penicillin therapy were few. A rash occurred in a patient with terminal carcinoma, who died a few days later. A rash also developed in a patient with Vincent's infection of the mouth, who had previously taken penicillin orally. Few patients complained of discomfort at the site of injection, and there was no instance of induration or abscess formation. Members of the house staff experienced little difficulty in the administration of penicillin.

SUMMARY

1. Aqueous procaine penicillin in amounts of 200,000 to 300,000 units injected twice daily gave a minimum sustained blood level in the range of 0.16 to 1.28 units per cubic centimeter, which was adequate therapy for many of the usual bacterial infections.

2. Adequate sustained penicillin blood levels necessary for therapy of more resistant bacterial infections were attained by injection twice daily of larger amounts of aqueous procaine penicillin.

3. Renal insufficiency tended to elevate penicillin blood levels because of decreased excretion, and cardiac failure tended to depress penicillin blood levels presumably because of poor absorption.

4. In this series few unfavorable side reactions and a high degree of patient acceptance were encountered. Twice daily administration of the drug facilitated nursing care.

Clinical Notes, Suggestions and New Instruments

OCULOGLANDULAR TULAREMIA TREATED WITH AUREOMYCIN

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The first of the newer antibiotics to show a striking activity against Pasteurella tularensis was streptomycin, as reported by Heilman[1] in 1944. To the present time this drug has been the treatment of choice. Since the oculoglandular form of tularemia is the unusual manifestation of this disease, only 87 cases being reported in the literature in the United States to 1947,[2] practically all the investigative work has been done on the other forms of the disease.

In 1947 Minden and Springer[2] reported a case of oculoglandular tularemia treated with streptomycin. In their case the temperature began to fall after twenty-four hours, reaching a normal level on the fourth day of therapy. A mild conjunctivitis and small palpable regional nodes were present after the fifth day. However, a low grade fever returned and was present for thirty days despite further treatment.

Aureomycin, isolated by Duggar,[3] was first reported in the treatment of tularemia by Woodward, Raby, Eppes, Holbrook and Hightower.[4] They found that aureomycin apparently has a more effective action against Past. tularensis in mice than streptomycin and that chloramphenicol (chloromycetin®) was the least effective of the three. Later Woodward[5] used aureomycin in 3 cases of human tularemia. One was the ulceroglandular form complicated by bilateral pneumonia, and the other 2 were the typhoidal type, both with pneumonia. In these cases the average duration of fever was 2.5 days after the start of therapy.

The following case is of interest because up to the time of writing there had been no report of the treatment of oculoglandular tularemia with aureomycin.

REPORT OF CASE

History.—I. R., a Negro farm laborer aged 32, was admitted to Kennedy Veterans Administration Hospital July 12, 1949 with swelling of the right eye and of the right side of the face and with fever and chills of four days' duration. Five days prior to admission an irritation began to develop in the right eye. The next morning the lids were decidedly swollen and the man felt feverish. He saw his local physician, who prescribed eye drops and penicillin. Throughout the day he had intermittent fever and chills. On the third day he noticed that his face was swollen in front of his right ear and below his right jaw. The following day the swelling had increased.

Fig. 1.—Oculoglandular tularemia. The palpebral conjunctiva shows scattered necrotic ulcers.

Examination.—On admission, the patient appeared to be a well developed man in acute distress. The temperature was 102 F., the pulse rate 90 and the respiratory rate 22. The right eye was swollen and tender. There was edema of both lids with a red, beefy hypertrophy of the palpebral conjunctivas. On the right upper palpebral conjunctiva were scattered eight small, discrete, shallow ulcers with yellowish bases (fig. 1). A few similar, smaller lesions were noted on the lower lid. There was a pronounced chemosis of the bulbar conjunctiva with several superficial corneal opacities, some of which stained with fluorescein. The pupil was normal. The refracting media were clear. The fundus was normal except for two small, old, pigmented areas with overlying retinal vessels. The right eye was normal.

The right preauricular, submental and submaxillary glands were enlarged and tender. There was no other significant adenopathy. The rest of the examination revealed essentially normal conditions.

From the Section of Ophthalmology, Veterans Administration Medical Teaching Group, Kennedy Hospital.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Heilman, F. R.: Streptomycin in Treatment of Experimental Tularemia, Proc. Staff Meet., Mayo Clin. **19**: 553-559 (Nov. 29) 1944.

2. Minden, P., and Springer, J. E.: Oculoglandular Tularemia Treated with Streptomycin, J. A. M. A. **134**: 1061-1064 (July 26) 1947.

3. Duggar, B. M.: Aureomycin: A Product of the Continuing Search for New Antibiotics, Ann. New York Acad. Sc. **51**: 177-181 (Nov. 30) 1948.

4. Woodward, T. E.; Raby, W. T.; Eppes, W.; Holbrook, W. A., and Hightower, J. A.: Aureomycin in Treatment of Experimental and Human Tularemia, J. A. M. A. **139**: 830-832 (March 26) 1949.

5. Woodward, T. E.: Chloromycetin and Aureomycin: Therapeutic Results, Ann. Int. Med. **31**: 53-82 (July) 1949.

Clinical Diagnosis.—Because of the typical clinical picture characterized by discrete necrotic ulcers of the palpebral conjunctiva, regional glandular involvement and systemic disturbance, a prelaboratory diagnosis of tularemia was made. Further investigation into the history revealed that the patient had recently handled several baby rabbits and that he had a pet dog that runs in the woods and probably catches wild rabbits.

Laboratory Diagnosis.—Direct smears from the conjunctival lesions showed only a few pus cells and rare gram-positive cocci. Blood culture and cultures of material from the lesions were negative on cystine hemoglobin agar. The result of a serum agglutination test for tularemia was negative on admission, positive in 1:80 and 1:160 dilutions five days later, and 1:2,560 two weeks after admission.

Clinical Course.—The patient's temperature varied from 102 to 103 F. during the first two hospital days. On the third day treatment with aureomycin, 500 mg. every six hours systemically, and aureomycin hydrochloride ophthalmic solution, locally every three hours, was started. Twelve hours after the first dose was administered there was a prompt and dramatic drop in temperature to normal, as shown in the accompanying chart (fig. 2). The temperature remained normal throughout the

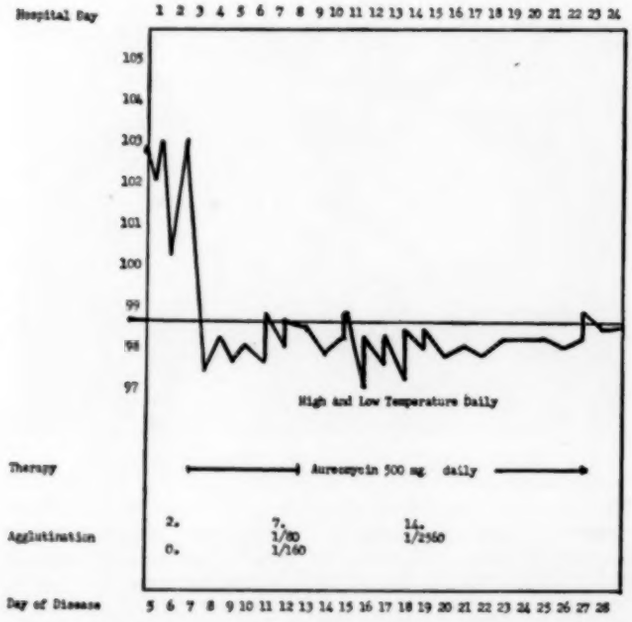

Fig. 2.—Clinical course of a man aged 32, 72.7 Kg., with oculoglandular tularemia.

patient's period in the hospital. After twenty-four hours there was a definite diminution in the swelling and tenderness of the eye and regional lymph nodes. One week later there was only a mild palpebral conjunctivitis and small palpable regional lymph nodes. Aureomycin therapy was continued for three weeks systemically and fifteen days locally. The patient complained of slight nausea, and a proprietary colloidal suspension of aluminum hydroxide was administered with the drug. The palpable lymph nodes were the last of the clinical observations to subside, disappearing completely by the time the drug was discontinued.

SUMMARY AND CONCLUSION

A case of oculoglandular tularemia is reported, which is probably the first in which aureomycin was used. A prompt and dramatic improvement in the ocular and systemic condition occurred, with the temperature falling to normal twelve hours after the onset of treatment. There was no further elevation of temperature.

Further investigation may prove aureomycin to be the drug of choice in tularemia.

Council on Physical Medicine and Rehabilitation

This paper was prepared at the request of the Council and is one of a series appearing in THE JOURNAL. *Later the entire series will appear in book form as the Council's Handbook of Physical Medicine and Rehabilitation.*

HOWARD A. CARTER, *Secretary.*

THE PHYSIOLOGIC ASPECTS OF THERAPEUTIC PHYSICAL EXERCISE

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A casual observation of a normal person in the midst of a feat of physical exercise impresses on one the important fact that all the systems of the body act in a nicely integrated manner toward an efficient achievement of unified action. During mobilization of the human body for physical activity, coordination of functions is of paramount importance.

The optimal effects of physical exercise are attained when oxygen is efficiently, sufficiently and continuously provided through the respiratory system, fuel is generously made available for the various tissues, especially the muscles, impulses through the central nervous system are sent to the skeletal musculature in a coordinated and integrated manner, and the waste products are completely eliminated without overtaxing the excretory organs or causing any disturbance in the acid-base, electrolyte and water equilibria in the organism.

SALIENT ANATOMIC FEATURES OF SKELETAL MUSCLE

Since skeletal muscles give the most vivid evidence of the physiologic effects of physical training, a discussion of their salient anatomic features is quite appropriate before the physiology of physical exercise is detailed.

The skeletal muscles make up about 50 per cent of the body weight of man. Each muscle is composed of many thousands of muscle fibers lying practically parallel one to the other. The individual fibers are bound together and are enclosed by a delicate connective-tissue sheath. About a dozen or more muscle fibers are grouped together in the form of a bundle (fasciculus). The whole muscle, composed of many fasciculi, is ensheathed by a fascia made of fibrous connective tissue. This strong framework of connective tissue becomes attached to the periosteum either directly or by forming a tendon at each end of the muscle through which it is attached to the periosteum of the bone.

The individual muscle fibers are cylindrical or prismatic in form with tapering ends. Each muscle fiber is composed of a fluid portion, the sarcoplasm (muscle cytoplasm) and a large number of myofibrillae or sarcostyles, which are the contractile elements.[1, 2] The wall of the muscle fiber is made of a homogeneous elastic sarcolemma, inside which several nuclei are scattered. Microscopic examination of fresh skeletal muscle fibers reveals the presence of both longitudinal and transverse striations. The transverse striations are produced by

1. Jordan, H. E.: The Structural Changes in Striped Muscle During Contraction, Physiol. Rev. **13**: 301-324 (July) 1933.
2. Speidel, C. C.: Studies of Living Muscles: II. Histological Changes in Single Fibers of Striated Muscle During Contraction and Clotting, Am. J. Anat. **65**: 471-529 (Nov.) 1939.

the alternate light and dark bands present in the muscle fibers and lying across the fiber in the same level in adjacent fibrils.

TYPES OF SKELETAL MUSCLES

On the basis of color, skeletal muscles are divided into two types, red and white (pale). The relative amount of sarcoplasm in the fibers varies. The color of muscle depends on the amount of pigment present. The red muscle contains enormous amounts of pigment granules (muscle hemoglobin), which give it the reddish appearance. Red muscles are capable of slow, powerful and long-continued contractions. The diaphragm and extensor muscles (postural) are good examples of predominantly red muscles. Such muscles that are engaged in powerful, slow and repeated movements are not easily fatigued and may contain more than one per cent of muscle hemoglobin, which is endowed with the property of combining more readily with oxygen than blood hemoglobin. Muscle hemoglobin furnishes an excellent local store for oxygen. Red muscles are more granular, less distinctly cross striated and less irritable, but give a stronger and more maintained contraction than pale fibers. White (pale) fibers are specialized for speed rather than strength of contraction. The rapidly acting muscles, such as breast muscles of birds and also flexor muscles in general, contain high concentrations of cytochrome oxidase systems, which are primarily concerned with the activation of molecular oxygen and its utilization in oxidative processes. Flabby muscles are believed to become pale as a result of rapid loss of myoglobin consequent to paralysis.[3] The muscles of man are made up mostly of the two types of fibers, namely, red and white; the relative predominance of one or the other varies according to the function of the muscle.

NERVE SUPPLY OF SKELETAL MUSCLE

The individual muscle fibers are so insulated from each other by the sarcolemmal sheath that stimulation of one fiber does not directly affect adjacent fibers. Consequently, in order to arouse a muscle fiber to action voluntarily, messages in the form of impulses must be sent to it along the motor nerve twig which penetrates its sarcolemma. Each muscle fiber is supplied by a separate branch from a motor nerve. As this nerve fiber penetrates the sarcolemma, it breaks up into several ramifications which terminate in a specialized mass of myoplasm known as the motor-end plate. When a single anterior horn cell in the spinal cord discharges impulses to a muscle, a certain group of muscle fibers, ranging between 100 and 200 in number, contract together as a unit. The axon of a motor nerve cell and all the 100 to 200 muscle fibers supplied by its ramifications form what is recognized as a motor unit. This is the basic functional neuromuscular unit which is believed to correspond to the fasciculus in muscle.

It must be kept in mind that in addition to the motor nerve supply, skeletal muscles are also provided with sensory nerve endings embedded in the connective tissue framework between the muscle fibers and in association with the tendons. These are stimulated by changes in tension in the muscle. During contraction, relaxation or stretch of the muscles, sensory nerve impulses are carried to the higher centers, conveying information of the state of the muscle and of the position of the parts of the body with respect to one another. The maintenance of muscle tone is dependent on such impulses.

There is no positive evidence for the existence of direct sympathetic nerve supply to skeletal muscle, as claimed by some; however, the consensus is that the sympathetic fibers present in muscle are vasomotor to the blood vessels. The existence of trophic fibers has yet to be proved. It is still in the battleground of speculation.

BLOOD SUPPLY OF SKELETAL MUSCLE

Muscle is richly supplied with blood. Each muscle receives blood through one or more arteries which branch freely and provide an extensive capillary network in the connective-tissue framework, supporting the individual muscle fibers. The sarcoplasm of the muscle fiber is separated from the blood in the lumen of the capillary by only the thin sarcolemmal sheath and the capillary endothelial wall. This provides means for efficient exchange of nutritive materials and wastes between the blood and the muscle. Capillaries are so abundant that an estimate of 4,000 per cubic millimeter of muscle cross section is given.

The distribution of the venous channels in muscle follows that of the arterial. Veins, however, are richly equipped with valves, including their minutest branches. This provides a unidirectional flow of venous blood (toward the heart) by compression of the veins during muscular contraction. This is the basis for the implication of the "milking" action of muscles in reference to the venous circulation.

Krogh[4] reported a great increase in the number of patent capillaries in activated muscles. Petrén and co-workers[5] noted an increase of about 45 per cent in the number of capillaries in guinea pig muscles during exercise as compared with those that were not exercised. They suggested that the increase in bulk of muscle during training is due to the increase in the number of capillaries. During inactivity many of these capillaries are closed, but more and more of them become patent as muscular activity increases. In this way the blood supply to a muscle is adjusted in accordance with the degree of vigor of muscular activity so that it insures a better circulation and supply of oxygen and a more efficient disposal of wastes.

THE ROLE OF THE NERVOUS SYSTEM IN MUSCULAR ACTIVITY

In a normal person muscular activity is brought about by impulses originating in the central nervous system. The principle underlying the development of motor skills is primarily perfection of the speed and accuracy with which the nervous system coordinates and correlates muscle action.

Postural contractions, including muscle tone, and phasic contractions, including reflex and volitional movements, are the two fundamental types of neuromuscular activity.

Muscle Tone.—Intact skeletal muscle with normal connections to the central nervous system displays a slight firmness in the form of sustained contraction usually recognized as muscle tone. Muscle tone is most evident and is easily demonstrated in the antigravity muscles; namely, those responsible for keeping

3. Schneider, E. C.: Physiology of Muscular Activity, ed. 2, Philadelphia, W. B. Saunders Company, 1939, p. 428.

4. Krogh, A.: The Anatomy and Physiology of Capillaries, ed. 2, New Haven, Connecticut, Yale University Press, 1929, 422.

5. Petrén, T.; Sjostrand, T., and Sylvén, B.: Der Einfluss des Trainings auf die Häufigkeit der Capillaren in Herz- und Skeletmuskulatur. Arbeitsphysiol. 9: 376-386 (July) 1936.

the head erect and the jaw closed, and those which prevent the body from sagging at the joints, especially hip and knee.

Muscle tone is believed to be reflex in nature with the sensory side of the reflex arc residing in the proprioceptors located in the muscles (muscle spindles) and in the tendinous attachments of muscles to bones (tendon organs). These proprioceptors are stimulated by tension or pressure. Consequently, when a muscle is stretched, impulses are sent up to the central nervous system, along the sensory nerve fibers whose endings are in the muscle spindles and tendon organs, and bring about a stimulation of the motor nerve cells whose efferent impulses are conveyed to the muscle fibers and induce contraction of that muscle. This stretch reflex is a fundamental factor in muscle tone and is usually well developed in the antigravity muscles (extensors). It is mainly responsible for the maintenance of body posture. Preservation of an upright posture is brought about by reflex contraction of the extensor muscles whose proprioceptors are stimulated by the stretch, and consequently prevent the knee joint from buckling.

Even though muscle tone is reflex in nature, the influence of the higher centers on posture and muscle tone is of paramount importance. An unconscious person, whether in sleep or fainting, has control neither over muscle tone nor over posture—his body crumples under its own weight. In a man deprived of his higher centers, the basic reflex mechanisms may be intact, yet he is unable to maintain normal posture.

In the maintenance of balance or equilibrium, the higher centers from the cerebral cortex, cerebellum and proprioceptors of the inner ear either increase or diminish muscle tone as the condition demands. Whenever the maintenance of equilibrium is threatened, reflexes from the retina, the labyrinth of the internal ear, and the muscle spindles of the muscles of the neck and extremities initiate corrective movements which restore normal posture and equilibrium.

Phasic Contractions.—Whether reflex or volitional, phasic contractions produce movement. Volitional contractions are involved in the development of motor skills. In the initial stages, before skill is attained, great attention is devoted to the component movements in a skilled act. These are controlled by the motor area. Visual and proprioceptive mechanisms aid in the necessary adjustments of strength and extent of movements. With practice the proper sequence of the various components of skilled movements are learned and attention is no longer required. Finally the act is performed entirely by proprioceptive guidance.

TYPES OF CONTRACTION OF A MUSCLE

The response of a muscle to a single stimulus is known as simple contraction. The duration of the contraction varies considerably in different animals and in different muscles of the same animal. It varies from one second in the terrapin to 0.1 second in the frog, to 0.003 second in insects, to 0.07 second in the rabbit. This is in skeletal muscles.

Isotonic Versus Isometric Contraction.—If the muscle is allowed to contract and shorten while contracting, such a contraction is *isotonic*. A portion of the energy liberated is converted into work by lifting the load. If the muscle is allowed to contract against a resistance too great for it to overcome, it cannot shorten and, therefore, the length of the muscle remains the same and the contraction is spoken of as *isometric*. The portion of the energy corresponding to that in doing work in the isotonic contraction now is utilized in developing tension in the isometric contraction. Fenn [6] proposed a classification which provides a better framework for the study of muscle. He classified muscle contractions into three categories: (1) tension during shortening; this accelerates or raises load, gives positive work, and positive excess energy; (2) isometric tension; this provides fixation, no work, and no excess energy; and (3) tension during lengthening; this decelerates or lowers load, gives negative work and negative excess energy.

Several types of contraction relative to muscular function should be viewed. When contraction of muscle produces decrease of distance between its origin and insertion, the process is known as a "shortening contraction" or a "concentric contraction." This type of contraction overcomes gravity or resistance and produces motion. During this contraction, either both ends of the muscle will move toward each other or, if one attachment of the muscle is fixed, the other attachment will be moved. This action then can have various effects, the origin of a muscle can be moved or, reversing the movements of the parts, its insertion can be moved.

Another type of contraction is known as "eccentric," or "lengthening," contraction. In this type of contraction outside forces cause the movement and the muscle regulates the speed at which the outside force may move the part. The muscular force constitutes a braking action. An example would be that of the flexed forearm being pulled down by the weight of the forearm and hand. The triceps does not act at all to produce extension, but the biceps brachii increases its length while, nevertheless, braking the speed of movement. This action is of considerable significance in coordination and in regulation of speed of a movement in which the part already in motion may exert considerable momentum.

If a muscle acts "to take up slack" but does not produce motion, the action is known as a "static contraction" and is primarily stabilizing in its effect. Other examples of such action are numerous in the co-ordinated muscular movement of the body; for instance, the stabilizing contraction of the gluteus muscles to prevent pelvic tilt in the process of taking a step, or contraction of the extensor muscles of the wrist in order to stabilize the hand when flexion of the fingers occurs.

Another muscular action which is of importance in relation to co-ordination is that known as "guiding action." During this action, muscle does not actually perform motion but controls the direction of motion.

CHEMICAL COMPOSITION OF MUSCLE

The proteins of muscle are myosin, globulin, myogen, actin and stroma-protein. Myosin is considered as the contractile substance of muscle.

Skeletal muscle contains 0.5 to 1 per cent glycogen. Glycogen is the chief carbohydrate of muscle and is its store of readily available foodstuff. It is in special relation to the contractile mechanism and to the enzyme systems that are thrown into action when the muscle contracts. Also phosphocreatine is present in amounts of 400 mg. per 100 Gm. Phosphocreatine is easily hydrolyzed to creatine and inorganic phosphate. This is strongly exothermic. The concentration of phospho-

6. Fenn, W. O., cited by Lloyd, D. P. C.: Functional Activity of Muscle, in Fultin, J. F.: Howell's Textbook of Physiology, ed. 15, Philadelphia, W. B. Saunders Company, 1946, chap. 2, p. 32.

creatine is highest in cardiac muscle and least in smooth muscle. Adenosine triphosphate is another labile organic phosphate present in muscle. In the hydrolysis of phosphocreatine and adenosine triphosphate, a large amount of energy is set free, appearing as heat. These are regarded as the compounds in which chemical energy is stored. They are the energy reserves.

CHEMICAL CHANGES IN MUSCLE DURING CONTRACTION

Muscular contraction is associated with the metabolic breakdown of certain chemical compounds. In spite of voluminous literature on the chemistry of muscle contraction, no crystallization of any opinions or definite conclusions can be made as yet. However, the consensus of most recent evidence suggests the following simplified sequence of chemical events during muscular contraction and recovery: (1) The breakdown of adenosine triphosphate supplies energy to initiate the muscular contraction which is believed to be due, among other things, to a physical alteration of the protein myosin.[7, 8, 9] (2) Breakdown of phosphocreatine supplies the energy required for the resynthesis of adenosine triphosphate. (3) The breakdown of glycogen to lactic acid provides the energy needed for the resynthesis of phosphocreatine. (4) Approximately a fifth of the liberated lactic acid, or the carbohydrate resulting therefrom, is oxidized to provide energy for the resynthesis of glycogen from the remainder of the lactic acid produced. Oxygen is essential for the last step.

ENERGY TRANSFORMATION IN MUSCLE

When muscles contract, energy is liberated. The liberation of energy occurs as a result of the chemical reactions which take place within the muscle fibers. Lactic acid production from glycogen is one of the fundamental chemical reactions which give energy for muscle contraction. Resting muscle contains very little lactic acid (about 0.02 per cent). With the muscle in nitrogen and at rest, lactic acid is slowly produced to a maximum of about 0.4 per cent at death of the muscle in rigor. The fatigued muscle, placed in oxygen, recovers its irritability, and lactic acid disappears. Muscles resting in oxygen retain their irritability for long periods, and no lactic acid accumulates. As stated above, lactic acid production is one of the fundamental chemical reactions that produce energy for muscle contractions. The reaction does not require oxygen. Muscular contraction is essentially an anaerobic process. Oxidative removal of lactic acid is necessary, since its accumulation in muscle leads to loss of irritability.

Muscle can produce large amounts of energy for a limited time in the absence of oxygen. One source of this energy is the partial decomposition of glycogen to lactic acid. Muscle requires oxygen for maintenance of normal irritability, for oxidative energy production and for the restoration of its anaerobic energy-yielding systems.

The formation of lactic acid from glycogen is accompanied with a large change in free energy. The free energy produced during the transformation of a glucose unit to glycogen and again to carbon dioxide and water is supposed to be about twelve times the free energy of glycolysis alone.

During exercise relative oxygen insufficiency develops and blood lactic acid rises, indicating that muscles are deriving energy from glycolysis. Later in the steady state of adequate oxygen supply, the blood lactate may be unchanged or may fall. No lactic acid accumulates after the oxygen supply becomes adequate to meet the energy requirements. After exercise, oxygen consumption does not at once return to the resting level. There is oxidative recovery, associated with removal of lactate and the refilling of the energy stores (resynthesis of phosphocreatine, formation of glycogen from glucose and lactate). The ability of muscle to accumulate oxygen debt is very useful.

Oxygen debt is the amount of oxygen used (over the resting amount) during recovery from exercise. This may be as high as 16 liters. The ability to go into oxygen debt is dependent, in part, on lactate production. Amounts as high as 204 mg. per 100 cc. (normal 10) have been recorded. A certain amount of oxygen debt may be incurred without the appearance of lactate in the blood. But when the oxygen debt reaches 3 or more liters, there is a direct relationship between the amount of lactate in the blood and the magnitude of oxygen debt.

The recovery period, therefore, is made up of two phases, an alactacid debt which is related to oxidation of usual food materials metabolized for the production of energy and the lactate debt related directly to oxidation of lactate.

During muscular exertion there are two phases: (1) initial rise and (2) "steady state." In the initial states the metabolism does not rise immediately to the final plateau because there is a slight lag in the circulatory and respiratory adjustment at the beginning of exercise.

The steady state is the condition in which the intake of oxygen meets the needs of the muscle. With severe exercise the intake of oxygen no longer keeps pace with the metabolic needs. Therefore, the first limiting factor is the maximal amount of oxygen a person can take per minute. This is conditioned by the efficiency of the respiratory and circulatory systems. The second limiting factor is the ability of the body to withstand lactate production.

Muscle Hemoglobin.—Muscles may contain about 1 per cent hemoglobin which is almost saturated with oxygen at the oxygen tension of venous blood (40 mm. of mercury) and is loaded at the low tensions in cells most remote from capillaries. Muscle hemoglobin provides a local store of oxygen in sustained contractions when the blood flow of tensed muscles is interrupted. The hemoglobin of muscle (myoglobin) takes oxygen much more readily than does blood hemoglobin. At an oxygen tension of 40 mm. of mercury, muscle hemoglobin is about 94 per cent saturated, whereas blood hemoglobin is only 60 per cent saturated. In rapidly acting muscles, rapid oxygen utilization is assured by increased concentration of enzymes (cytochrome oxidase systems).

The various current views can be summed up as follows: Glycolysis and oxidation in muscle are directed mainly toward the production of phosphate bond energy. Potential energy in this form is made available to the "contractile system" in order of immediacy, through the breakdown of adenosine triphosphate and phosphocreatine.

In activity, the initial energy requirements are met by adenosine triphosphate and phosphocreatine, but

7. Engelhardt, W. A., and Ljubimowa, M. N.: Myosine and Adenosinetriphosphatase, Nature, London **144**: 668-669 (Oct. 14) 1939.
8. Needham, Dorothy M.: The Adenosinetriphosphatase Activity of Myosin Preparations, Biochem J. **36**: 113-120 (Feb. 6) 1942.
9. Bailey, K.: Myosin and Adenosinetriphosphatase, Biochem. J. **36**: 121-139 (Feb. 6) 1942.

glycolysis and oxidation accelerate rapidly to meet the continuing energy requirements during activity.

Iodoacetic acid inhibits the oxidation of phosphoglyceraldehyde, and no lactic acid can be formed.

Muscles poisoned with iodoacetic acid could contract vigorously for a time before going into rigor without producing any lactic acid. In these circumstances, phosphocreatine breakdown is the principal unreversed energy-yielding reaction. Since phosphocreatine serves as the reservoir of bond phosphate for resynthesis of adenosine triphosphate, the latter must break down first when the muscle contracts.

Myosin is now believed to form the structural basis of the muscle machine and it is believed to be closely linked with the breakdown of adenosine triphosphate, involving a large turnover of energy. The breakdown of adenosine triphosphate is the reaction nearest in time to the physical process of contraction. Addition of adenosine triphosphate to muscle increases its sensitivity not only to subsequent doses of acetylcholine but also to electrical stimulation in curarized muscles.

Heat Liberated During Muscle Contraction.—An activated muscle becomes warm. The amount of heat liberated is estimated in terms of calories. Analysis of records shows that heat is liberated in two portions: (1) initial heat and (2) delayed heat.

Initial heat is a sudden outburst at the very beginning of contraction and a slower but small portion during relaxation. Delayed heat occurs, after contraction and relaxation are over, during the period of recovery.

The initial heat is due to the chemical changes in the muscle liberated by the stimulus. This output of heat takes place in the complete absence of oxygen and hence must be due to nonoxidative reactions.

The initial heat consists of two phases: (1) a sudden outburst which occurs at the very beginning of contraction and is practically over in 0.1 to 0.2 second; this is designated as the "contraction heat" and is associated presumably with dissociation of phosphocreatine; and (2) the smaller and more gradual heat production which takes place during relaxation or fall of tension and is called "relaxation heat"; this is due to dissipation, in the form of heat, of the mechanical potential energy of tension. It represents 35 per cent of the initial heat.

The delayed heat, at least in part, depends on the presence of oxygen. If the muscle is stimulated in an atmosphere of nitrogen, most of the delayed heat drops out. Delayed heat consists of two parts or phases; namely, (1) the anaerobic delayed heat which appears immediately at the end of the contraction and may be detected in either the presence or the absence of oxygen; it is small in amount, representing about 8 per cent of the initial heat; and (2) the oxygen recovery heat, which is much larger in amount, appears later and is lacking in the absence of oxygen. It depends on oxidative changes taking place in the muscle during the recovery period after the contraction is over. It is due to oxidation of lactic acid, the synthesis of phosphocreatine and the synthesis of lactic acid to glycogen.

If a muscle lifts a load, work is done which can be expressed in kilogram-meters, foot-pounds or any other convenient unit indicating the product of a weight by a height. The result can also be expressed in different terms by using the "mechanical equivalent of heat," namely, the fact that 426.5 kilogram-meters equal one large calorie.

If a muscle contracts against a strong resistance and cannot shorten, the work done is more difficult to measure directly. Since the tension, however, is dissipated as heat, one can determine the heat in calories and so obtain an indirect measure of the work.

ACTION OF MUSCLES IN THE BODY

Most of the voluntary contractions are too long continued to be simple contractions. The time element alone would place them in the group of tetanic contractions. Even the shortest possible voluntary contractions are brief tetanic contractions made up of a short-lasting series of contractions fused together.

Skeletal muscles act in the body by producing rotation of bony levers at the joint articulations. The lever system of the body is acted on by many external forces, including gravity, counterpressure of the floor and floor friction. To meet these forces, muscles must exert opposing forces in order to prevent movement and to maintain position.

In general, muscles are arranged in antagonistic pairs, about a joint, an arrangement which permits rotation of the levers in both directions through the utilization of muscle tension.

In a voluntary muscular act, four groups of muscles are concerned:

1. *Prime movers or agonists.* This comprises those muscles whose contraction is essentially responsible for the movement of a part.

2. *Antagonists* oppose the agonists.

3. *Synergists* assist the agonists and reduce unnecessary movement to a minimum.

4. *Fixation muscles* whose contraction causes the fixation of neighboring joints and maintains the part in a position appropriate for doing the act.

EFFICIENCY OF MUSCLE AS A WORK MACHINE

Efficiency indicates what percentage of the total energy given to an engine or developed in the engine may be obtained as external or mechanical work. If Q equals total energy developed, W equals the energy (expressed in the same unit) obtained as work and E equals efficiency, then E equals $\frac{W}{Q}$.

Efficiency varies in different muscles and in the same muscle under different conditions. In very slow or very quick movements the efficiency is low, so that for any given task there is a certain rate at which the work can be done most economically.

The efficiency of human muscle ranges from 21 to 25 per cent. In determining the work done, one must apply the formula: work equals load times distance. If either load or distance is zero, no work is done. Also, there is an optimal load for each muscle with which the greatest proportion of work can be obtained. What measures the absolute power of a muscle? It is measured by the weight which the muscle cannot lift, and which, on the other hand, cannot cause any extension of the muscle while contracting. The absolute power of a muscle is the maximum of tension which it can reach without alteration of its natural length.

PHYSIOLOGIC EFFECTS OF MUSCULAR EXERCISE

Any observer realizes that strenuous muscular exertion leads to breathlessness, increase in heart rate, rise in body temperature and fatigue; but it takes a trained medical observer to be able to judge from the strenuousness of the exercise and the response of the person taking it as to how fit or unfit a man may be.

Under the influence of continued strenuous exercise, the oxygen consumption may rise from its resting value of 250 cc. per minute to a maximal value of 4 or more liters per minute; and in order to transfer 4 liters of oxygen from the lungs to the muscles, 34 liters of blood are required (100 cc. of blood carry about 18.5 cc. of oxygen, about 70 per cent of which is removed by the muscles). Consequently during severe exercise each side of the heart may have to pump 34 liters of blood per minute. Since the total volume of blood in the body is about 5 liters, it means that all the blood must circulate about seven times a minute. This indicates clearly that in severe exercise an enormous output of the heart is needed and any impairment in cardiac function is revealed by the inability of the subject to tolerate exercise of such severity. If the circulatory response to the demands of the muscles for oxygen during muscular exertion fails, the blood will be severely desaturated (deoxygenated) and cyanosis develops. But an adequate response of the circulation is associated with a considerable increase in heart rate and in arterial blood pressure to drive the blood along the vascular tree.

The mechanical efficiency of the human body is only 25 per cent. This means that only a relatively small fraction of the chemical energy derived from oxidation is transformed into external mechanical work. The remainder is converted into heat. Most of the extra heat produced during exercise is lost from the skin and lungs, but some of the heat remains in the body and raises the body temperature. The magnitude of this rise in body temperature depends on the severity of the exercise and on conditions, such as clothing, obesity and humidity of environment, all of which may delay dissipation of heat from the body. This rise in body temperature speeds up most of the processes in the body, metabolic and otherwise, among them the frequency of the heart beat.

The rate of performance of long-continued severe physical work is limited by the maximal rate of oxygen intake and the output of the heart. However, the body can incur an "oxygen debt" during a short spurt of violent exertion by postponing the oxygen intake equivalent to the excess work until the period of recovery from the exertion. This indicates the existence of a mechanism whereby the muscles can perform work for a short time without deriving energy from simultaneous oxidation.

During recovery from any form of exertion an excess of oxygen over the resting oxygen consumption is taken. This indicates that for even moderate exercise oxygen debt is incurred. The duration of the recovery period depends on the duration and severity of the exertion, and on the "fitness" of the subject. It may vary from a few minutes to an hour or more.

The excess oxygen intake during the recovery process is necessarily accompanied with a greater circulation rate, in order that the oxygen may be transported from the lungs and distributed to the muscles. Therefore, the frequency of the heartbeat is considerably greater during exertion than at rest. The duration of the persistence of an increased heart rate during recovery from exercise is a valuable indication of the rate of a man's recovery, and consequently his "fitness." It provides one of the convenient clinical tests by which the reserves of a patient may be recognized as in the pathologic or normal range.

The heart rate increases from the very onset of exercise and approaches a steady state in about two minutes. This initial increase is due largely to a nervous mechanism originating in the brain. It begins before the actual start of the exercise, during a period of anticipation of the action, and is due to influence from higher centers.

Delachaux and co-workers [10] reported that physical training produces changes, particularly in the lungs, circulatory apparatus and the products of cellular respiration. Some of these changes, they believe, protect the heart against overstrain. In well trained persons the peripheral resistance of the circulation is reduced, while a denser capillary network and a high intracellular hemin level create optimal conditions for metabolic exchange between blood and cells; consequently, the same amount of cardiac energy will supply more oxygen to the periphery in the trained than in the untrained. The heart muscle undergoes changes similar to skeletal muscle changes, greater vascularization and increase in intracellular hemin for carriage and storage of oxygen. The increase in respiratory products insures protection against oxygen deficiency during exertion. The heart hypertrophies, and, when intensive training ceases, the cardiac volume decreases gradually. Well trained athletes develop a definite bradycardia. During exercise their heart does not beat as fast as that of nonathletes. Müller [11] presented evidence that the bradycardia produced by training is due to peripheral changes in muscles; namely, better vascularization and oxygen utilization in the muscles used in training.

Schwartz and associates [12] demonstrated that systemic muscular exercise led to increase of height, weight and vital capacity of adolescent boys. In a study of the influence of exercise on the growth of organs in albino rats, Hatai [13] reported an increase of body weight and organ weights after continued exercise in cages for a period of six months. Born [14] studied a group of Yale men in their freshman and senior years. He concluded that systematic exercise increases body weight, shoulder breadth, vital capacity, girth and strength of the exercised muscles. Individual bones as well as the entire skeleton are modified by muscular exercise. Regular exercise increased the density of bones. Schneider [3] stated that a man in poor physical condition as easily exhausted by mental and physical exertion while a man in good physical state is mentally alert and physically vigorous and has bright eyes and a healthy complexion. Bainbridge [15] remarked that systematic exercise improves the whole muscular system and increases the range and delicacy of the adjustments of the respiratory and circulatory systems.

Following are some specific physiologic effects of coordinated and organized muscular activity on the muscles themselves.

1. *Muscle Structure.*—Regular and systematic exercise, especially when it is of a heavy nature, brings

10. Delachaux, A.; Mamie, M., and Aymon, G.: Le coeur dans l'entrainement physique et le surentrainement, Cardiologia **9**: 173-210, 1945.
11. Müller, E. A.: Die Pulszahl als Kennzeichen für Stoffaustausch und Ermüdbarkeit des arbeitenden Muskels, Arbeitsphysiol. **12**: 92-104 (March) 1942.
12. Schwartz, L.; Britten, R. H., and Thompson, L. R.: Studies in Physical Development and Posture: I. The Effect of Exercise on the Physical Condition and Development of Adolescent Boys; II. Bodily Growth With Age; III. Physical Fitness as Reflected in Tests of Muscular Strength, U. S. Pub. Health Bull. **179**: 1-124 (June) 1928.
13. Hatai, S.: On the Influence of Exercise on the Growth of Organs in the Albino Rat, Anat. Rec. **9**: 647-665 (Aug.) 1915.
14. Born, F. J., cited by Schneider.[3]
15. Bainbridge, F. A.: The Physiology of Muscular Exercise, London, Longmans, Green and Co., 1919, p. 215.

about definite changes in the structure of the muscles. It tends to thicken and toughen the sarcolemma of muscle fibers and also to increase the amount of connective tissue within the muscle. This is the basis for the tough and coarse meat of heavily worked animals as compared with those that were confined and inactive throughout their lives.

2. *Muscle Size.*—Muscular activity brings about a definite increase in the size of the whole muscle and of its individual fibers. This increase in size of the muscle is due partly to the improved circulation and partly to the chemical changes occurring during repeated activity of the muscles. Training does not increase the number of muscle fibers, but it brings about an activation of the unused fibers that have become small from lack of use. Consequently, these repeatedly activated fibers increase in size and become well developed. Some believe [8] that this increase in the size of the muscle is due to an increase in the number of capillaries resulting from the repeated exercise; and it is stated that the exercises of strength induce hypertrophy of the muscle fibers, and the exercises of endurance induce capillarization.[16]

3. *Increase in Strength.*—In order to develop strength of muscles, they must be exercised against gradually increasing resistance. It must also be remembered that the rapidity and ultimate degree of development of the muscles in different persons differs. Usually persons with small bones who are tall and thin, will reach the limit of development much sooner than a stocky person with larger bones. However, this is not the only explanation. There are other unknown factors that cannot be explained.

4. *Gain in Endurance.*—The increase in absolute strength of an individual or a group of muscles does not necessarily mean a gain in endurance. The strong man can perform work against greater resistance, but if the weights to be lifted or the exercise to be done is of medium load, a person with less powerful muscles may be the champion. Often it is found that the gain in endurance is out of all proportion to the gain in size of the muscle. It must be remembered that the increase in endurance is probably due to the improvement of the quality of contractions of the muscles, which is brought about by training. This improvement in quality is often associated with actual chemical changes, by means of which (*a*) the fuel for muscular activity may be made more available, or (*b*) the fuel is stored in greater amounts, or (*c*) the oxygen is more abundant because of a greater adequacy of circulating blood through the muscles. It has been shown that training which brings about a gain in endurance also leads to an increase in the number of capillaries in the muscles. Maison and Broeker [17] demonstrated that the endurance of muscles with adequate blood supply increased more rapidly and reached a higher level than those without adequate blood supply. Their experiments have suggested that important changes take place during exercise and that an adequate blood supply is essential for these changes.

5. *Chemical Changes.*—It has been shown experimentally on rabbits that the training of muscles for a period of five days was sufficient to bring about a definite increase in the phosphocreatine content.[18] Also, it has been shown experimentally that exercising the muscles invariably resulted in a greater content of glycogen.[19] Furthermore, the quantity of non-nitrogenous substances was increased during training, and the color of the trained muscles was darker than that of the untrained. This indicates a more favorable state for the transport and utilization of oxygen, because the color of the muscle is due to its hemoglobin content. Whipple [20] found that a greater amount of hemoglobin is present in the muscles of active dogs than in inactive ones. The muscles of active, trained dogs were found to contain up to 1,000 mg. of hemoglobin per 100 gm. of muscle, while in the quiet house dog the muscles contained about 400 mg.

6. *Facilitation of End-plate Transmission.*—Some have suggested that the facility of transmission of nerve impulses across motor end-plates in muscles is usually brought about by systematic muscular exercise. This is difficult to prove.

7. *More Nearly Complete Use of Muscle Fibers.*—It has been assumed, also, that as the end-plate transmission is improved and inactive fibers are brought into action it becomes much easier for the muscle fibers to be put into action in their entirety. This, of course, suggests that a muscle whose fibers have been brought into action altogether is much stronger than one containing many idle fibers.

8. *Increase in Number of Capillaries.*—In the heart and in the gastrocnemius muscle the number of capillaries was found to be 40 to 45 per cent more in the trained than in the untrained animals (guinea pigs). This led to the conclusion that the gain in endurance is mainly a problem of improving the transport of blood to the muscles through an increase in the number of capillaries.

The important physiologic effects of systematic physical exercise can be summarized as follows: (1) Effort can be withstood for a much longer period without exhaustion by the trained than by the untrained person. (2) The resting heart rate becomes so slow that a definite bradycardia occurs in well trained athletes. (3) Greater stroke volume of the ventricles makes it unnecessary for the heart to speed up considerably to cope with the demands of moderate exertion. (4) The heart rate and blood pressure return to resting levels much more rapidly on cessation of physical activity in the trained than in the untrained person. (5) Rate and depth of respiration during rest are usually slightly reduced in well trained athletes. (6) During moderate exertion pulmonary ventilation is not noticeably labored, and during exhausting work a greater minute volume of ventilation is attained in the trained than in the untrained person. (7) Oxygen utilization is more efficient and energy reserves are more effectively utilized anaerobically in the trained than in the untrained person. (8) The concentration of blood lactate does not rise very high during moderate activity and a higher concentration of blood lactate can be withstood for long periods without any signs of exhaustion during severe exertion in the trained than in the untrained person.

16. Schneider, E. C., and Karpovich, P. V.: Physiology of Muscular Activity, ed. 3, Philadelphia, W. B. Saunders Company, 1948, p. 22.

17. Maison, G. L., and Broeker, A. G.: Training in Human Muscles Working With and Without Blood Supply. Am. J. Physiol. **132**: 390-404 (March) 1941.

18. Palladin, A., and Ferdmann, D.: Über den Einfluss des Training der Muskeln auf ihren Kreatingehalt, Ztschr. f. Physiol. Chem. **174**: 284-294, 1928.

19. Embden, G., and Hoba, H.: Beitrag zur Lehre vom Muskeltraining, Skandinav. Arch. f. Physiol. **49**: 122-123 (Aug.) 1926.

20. Whipple, G. H.: The Hemoglobin of Striated Muscle, Am. J. Physiol. **76**: 693-707 (May) 1926.

Fatigue is a state during which a muscle fails to respond to stimulation. During the onset of fatigue a muscle relaxes more and more until it becomes completely unirritable. But a short interval of rest is sufficient to bring about some return of irritability. For complete restoration, a long interval of rest is necessary. Products of muscular activity accumulate in muscle and lead to depression of its irritability and contractility. Lactic acid is one of the important products. Other unknown products of muscular metabolism also have a similar effect. Accumulation of lactic acid in the muscle, and consequently in the blood, indicates that the oxygen supply to the contracting muscles is inadequate. The muscles accumulate an oxygen debt owing to their ability to contract anaerobically. The more strenuous the exercise, the more insufficient is the oxygen supply; this is indicated by a rise in the value for lactic acid in the blood. The supply of energy-yielding material has been depleted. The processes of restoration have not kept pace with those of consumption. In this sense there is a real exhaustion of the muscle. But fatigue appears on accumulation of lactic acid, while the muscle still contains energy-yielding material.

Extreme fatigue or exhaustion is normally prevented by the fact that the nerve centers and motor end-plates develop the phenomena of fatigue before the muscles themselves do and, therefore, there is hardly ever a condition of extreme exhaustion.

THE PHYSIOLOGIC BACKGROUND OF FATIGUE

Fatigued muscles lose irritability and contractility. This fatigue is due to the consumption of all available contractile materials and to the accumulation of fatigue products formed during metabolic activity. The presence of these products may be due either to overproduction of wastes or to faulty elimination. The faulty elimination may be due to maintained tetanic contractions or to interference with the circulation. It is important to keep in mind the fact that a muscle has the least blood supply and is least capable of eliminating its wastes and replenishing its nutritive elements during the contraction phase. Therefore, the less the contraction phase is maintained, the better is the outcome for the muscle.

The following parts are to be considered in fatigue: (1) the motor nerve cell, (2) the synapses, (3) the motor nerve fiber, (4) the motor end-plate and (5) the muscle itself. Regarding the nerve fiber, there is sufficient evidence to indicate that it does not fatigue readily. Its metabolism, even under activity, is exceedingly small. The synapses, the motor end-plate and the muscle itself are the seats of fatigue, especially the motor end-plate, which fatigues most easily. Experiments were made by paralyzing the end-plates with curare and then stimulating the nerve. Nerve stimulation was carried on for more than six hours, and as soon as the curare effect wore off muscular contraction appeared. This indicated that even continuous activation of the nerve for six hours did not fatigue it. The myoneural junction is generally held as a very important seat of fatigue.

Following are some of the major factors which influence the progress of fatigue. (1) Frequency of contraction. The greater the rate of activation of a muscle, the more rapid is the onset of fatigue. During contraction the muscle is least capable of replenishing its circulation. (2) The completeness of exhaustion. The more complete the exhaustion, whether it is mental or muscular, the longer is the period necessary for recovery. (3) The load. The greater the load, the more rapid the onset of fatigue and the smaller is the total amount of work done. Poor circulation reduces the working power of the muscle and causes it to fatigue earlier. (4) The work capacity is increased by rest, moderately low external temperature, training and massage. Increased arterial pressure also reduces fatigue. Strenuous work decreases muscle tone and brings about fatigue early.

Breathlessness.—Breathlessness is manifested during extremely strenuous exertion (1) when large groups of muscles are actively used, (2) when respiration is interfered with mechanically, or (3) when anxiety, fear and excitement are present, or when any two, or all three, conditions are in effect concurrently. Breathlessness is more likely to occur in persons who are not in good athletic trim or are in poor physical shape.

Lack of oxygen, great reduction of lung surface and limitation of thoracic movement (for example, thoracic disease, or ossification of the thorax leading to rigidity the limitations of excursions) cause breathlessness. Congestion of the pulmonary system and the other vessels in the thorax lessen the room for air.

The inability of the heart to bring the blood rapidly enough to the lungs or to take it to the tissues because of valvular lesion or weakened myocardium makes an important cause for breathlessness.

Chemical changes in the blood leading to an increased acidity, the rise in body temperature and the impulses from higher centers and from contracting muscles all drive the respiratory center to breathlessness. Accumulation of lactic acid in the blood is another factor causing breathlessness.

Second Wind.—Second wind occurs during vigorous exercise. The dyspnea and breathlessness diminish at a certain stage during severe work and the subject continues the exercise with greater comfort. The percentage of carbon dioxide in alveolar air decreases after second wind occurs.[21] With the arrival of second wind, cardiac distress disappears, the breathing becomes easier and sweating usually begins. The cause of second wind is unknown. Second wind may occur when sufficient oxygen is supplied to the muscles to eliminate the excess lactic acid. The increased temperature in the muscles would stimulate chemical processes. The larger flow in the dilated capillaries would bring oxygen to aid in the elimination of the lactic acid. Hartman and co-workers[22] suggested that the second wind and the warming up process are accompanied with an increase in the output of epinephrine. Hoskins and Durrant[23] demonstrated that epinephrine increased the activity of skeletal muscles.

Second wind is apparently an adjustment of all the coordinating mechanisms in the heart, lungs, muscles, metabolism, elimination and nervous system. Failure of any of these causes breathlessness. A trained athlete has complete adjustment of these mechanisms.

Muscle Pain, Soreness and Stiffness.—Muscle pain is characterized by aching. It is well known by those

21. Cook, F., and Pembrey, M. S.: Observations on the Effects of Muscular Exercises Upon Man, J. Physiol. (London) **45**: 429-446 (Feb. 5) 1913.

22. Hartman, F. A.; Waite, R. H., and Powell, E. F.: The Relation of the Adrenals to Fatigue, Am. J. Physiol. **60**: 255-269 (April) 1922.

23. Hoskins, R. G., and Durrant, E. P.: The Effect of Fatigued Muscle Upon Perfused Adrenalin, Am. J. Physiol. **66**: 176-179 (Sept.) 1923.

who have overused muscles unaccustomed to an activity for the first time on a previous day. The pain produced by injury to web, tendon, periosteum, joints and deep fascia is similar to muscle pain; it is deep, gnawing in character. Usually, muscles are known to ache and tendons to hurt.

All joint pain arises in synovial membrane, as articular cartilage is relatively insensitive. The pain of arthritis is deep and boring. Only pain in superficial structures is well localized. Pain in deep structures is poorly localized and it possesses two components, the primary pain and the secondary pain, but may be referred to another part of the body altogether. The deeper the source of the pain, the poorer is the localization.

Mechanism of Muscle Pain.[24]—The muscle spindles in muscle and the organs of Golgi in the tendons are stimulated by changes of tension, whether these are produced actively as a result of contraction or passively by means of stretch. Stimulation of receptors other than those specifically concerned with pain cannot give rise to pain sensations. Little is known about the pain nerve endings in muscle. Hinsey [25] reported that free nerve endings are found around the blood vessels in muscle and in the aponeurotic sheaths and subserve pain in these localities. The mode of action of sensory organs in skin as well as in muscle is explained by the presence of specific types of nerve endings which respond to an appropriate and specific stimulus and to none other. There is doubt whether the cortex mediates pain sensation; it is more probable that the seat of pain is mainly in the thalamus. The intensity of the sensation depends on the frequency of the impulses set up in the peripheral sense organ. The extent of the area stimulated is judged from the number of afferent fibers simultaneously activated.

Three types of somatic pain are recognized: they come from skin, muscle and tendon, respectively. Muscle pain, with which we are especially concerned here, could be continuous, diffuse and difficult to locate. It is different from skin pain. It can be produced by exercising a muscle under ischemic conditions, squeezing a muscle violently, or injecting into it hypertonic or acid isotonic saline solutions. Muscle pain may be referred to distant parts. Stimulation of tendon or periosteum produces similar pain to the type known as web pain, which is elicited by pinching the short web of skin between adjacent fingers. Kellgren [26] reemphasized the presence of tender spots in myalgia or fibrositis, which, when pressed upon, give rise to diffuse widespread pain which is of a referred character. When the tender spots are infiltrated with a local anesthetic, both local and referred pain disappear. This may account for the beneficial effect of massage and of radiation therapy applied to localized tender spots which are probably the actual foci of the disease. Lewis [27] made a study of the mechanism of ischemic pain. He exercised the hand after entire occlusion of the circulation to the arm. Pain set in after about thirty seconds and became intolerable in seventy seconds. It was diffusely felt, but most marked in the muscles. It is not due to vascular spasm, because, after occlusion, the blood vessels lose their tone. It is not due to muscular tension, because it is continuous and is not accentuated during the phase of contraction. It is the result of activity, because it is related to the amount of exercise which is performed. It is not due to local anoxia. If the limb is exercised to a point short of pain and the occlusion kept up, no pain develops, although the anoxia becomes progressively more intense. Activity liberates a pain-producing factor (P) which normally passes into the tissue spaces and is removed by the blood stream. The substances accumulate in conditions of ischemia and give rise to pain.

Despite the fact that life is made miserable for hundreds of thousands by chronically stiff, aching muscles, very little is known about the altered physiology of diseased muscles even in common states, such as muscular rheumatism. Muscle biopsy is easily performed but the information obtained so far does not help. Physiologic reactions of muscles are fairly well known, but very little is known for the treatment or understanding of muscle diseases.

Muscle soreness is of two types: (1) general soreness due to the presence of diffusible waste products and (2) soreness due to ruptures within the muscle fiber or the fibrous covering and attachments of the muscle to the bones. The pain due to accumulation of waste products in the muscle is most severe during work. About one-half hour after the exercise the muscle is lame and sore to touch. The pain and discomfort gradually wear off during the first four hours after the exercise and then disappear completely.

The second type of soreness is not noticed during the exercise nor for several hours after the exercise. It begins toward the end of the day or on the second day after the activity when the muscles feel stiff and sore. The soreness may disappear in three or four days, or may last longer if the work was very severe. Boyle and Scott [28] stated that, although there are vascular and lymph changes in muscle as a result of exercise, this type of muscle soreness is not due to metabolic products accumulated in the muscle.

The general type of soreness is considered to be due to the accumulation of waste products within the sarcolemma and later within the interstitial lymph spaces. This edema of the muscle continues until the blood and lymph currents can remove the waste products from the muscle. Pressure of the swollen muscle fibers on the sensory nerve endings, or the chemical stimulation of these endings by the waste products, causes the soreness. Mild work through alternate contractions forces the waste products out of the area and allows fresh blood to enter with needed nutriment. Massage here helps.

The second kind of soreness is caused by rupture of muscle fibers which are less often used and are more susceptible to strain than the fibers regularly used in ordinary contractions. The persistence of the soreness may be due to the breaking up of adhesions between the injured fibers. This type of soreness needs rest and heat and only enough contractions to prevent adhesions between the sore muscle fibers. Slow contractions avoid tearing the adhesions and may stretch them without severe pain.

24. Wright, S.: Physiological Aspects of Rheumatism, Proc. Roy. Soc. Med. **32**: 651-662 (Jan. 20) 1939.

25. Hinsey, J. C.: Some Observations on the Innervation of Skeletal Muscle of the Cat, J. Comp. Neurol. **44**: 87-195 (Oct.) 1927.

26. Kellgren, J. H.: A Preliminary Account of Referred Pains Arising from Muscle, Brit. M. J. **1**: 325-327 (Feb. 12) 1938.

27. Lewis, T.: Pain in Muscular Ischemia; Its Relation to Anginal Pain, Arch. Int. Med. **49**: 713-727 (May) 1932.

28. Boyle, R. W., and Scott, F. H.: Some Observations on the Effect of Exercise on the Blood, Lymph and Muscle in Its Relation to Muscle Soreness, Am. J. Physiol. **122**: 569-584 (June) 1938.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

OFFICE OF THE SECRETARY.

DICUMAROL (See New and Nonofficial Remedies 1949, page 347).

The following dosage form has been accepted:

E. R. SQUIBB & SONS, NEW YORK 22

Capsules Dicumarol: 50 mg. and 0.1 Gm.

ESTROGENIC SUBSTANCES (WATER INSOLUBLE) (See New and Nonofficial Remedies 1949, page 367).

The following dosage forms have been accepted:

THE WM. S. MERRELL CO., CINCINNATI 15

Aqueous Suspension Proliculin: 10 cc. vials: A suspension in isotonic solution of sodium chloride containing 20,000 I.U. (2 mg.) of estrone in each cc. Preserved with thimerosal 1:20,000.

Solution Proliculin in Oil: 10 cc. vials: A solution in vegetable oil containing 20,000 I.U. (2 mg.) of estrone in each cc. Preserved with 0.5 per cent chlorobutanol. 20 cc. vials: A solution in vegetable oil containing 10,000 I.U. (1 mg.) of estrone in each cc. Preserved with 0.5 per cent chlorobutanol.

U. S. trademark 368,786.

REED & CARNRICK, JERSEY CITY, N. J.

Solution Estrogenic Substances in Oil: 10 cc. and 20 cc. vials: A solution in peanut oil containing 20,000 I.U. of estrone in each cc. Preserved with 0.50 per cent chlorobutanol.

PENICILLIN FOR PARENTERAL USE FOR PROLONGED ACTION (See New and Nonofficial Remedies 1949, page 153).

The following dosage form has been accepted:

THE UPJOHN COMPANY, KALAMAZOO, MICH.

Depo-Procaine Penicillin G in Oil: 1 cc. cartridges packaged with B-D disposable cartridge syringe and 10 cc. vials: A suspension in peanut oil containing 300,000 units of crystalline procaine penicillin G with 2 per cent aluminum monostearate.

PENICILLIN FOR ORAL ADMINISTRATION AND PENICILLIN FOR INHALATION THERAPY (See New and Nonofficial Remedies 1949, page 156 and page 157, respectively).

The following dosage form has been accepted:

SCHENLEY LABORATORIES, INC., NEW YORK 1

Soluble Tablets Crystalline Potassium Penicillin G: 50,000 units.

PENTOBARBITAL SODIUM-U.S.P. (See New and Nonofficial Remedies 1949, page 461).

The following dosage forms have been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Capsules Nembutal Sodium: 30 mg., 50 mg. and 0.1 Gm.

Powder Nembutal Sodium: 5 cc. ampuls: Each ampul contains 0.25 Gm. or 0.5 Gm. of pentobarbital sodium powder. 20 cc. vials: Each vial contains 0.5 Gm. of pentobarbital sodium powder.

Solution Nembutal Sodium: 5 cc. ampuls and 50 cc. vials: A solution containing 50 mg. of pentobarbital sodium in each cc.

Suppositories Nembutal Sodium: 30 mg., 60 mg., 0.12 Gm. and 0.2 Gm.

U. S. trademark 285,003.

TESTOSTERONE PROPIONATE-U.S.P. (See New and Nonofficial Remedies 1949, page 407).

The following dosage form has been accepted:

SCHIEFFELIN & COMPANY, NEW YORK CITY.

Solution Testosterone Propionate in Oil: 1 cc. ampuls and 10 cc. vials. A solution in sesame oil containing 25 mg. of testosterone propionate in each cc.

Council on Foods and Nutrition

The following products have been accepted as conforming to the rules of the Council.

JAMES R. WILSON, M.D., *Secretary.*

The Nestle Company, New York

PELARGON. Ingredients: Powdered whole milk, refined cane or beet sugar (sucrose), glucose (corn syrup), corn or potato starch, iron and ammonium citrate, and the added vitamins or vitamin precursors, carotene, thiamine hydrochloride, ascorbic acid and activated 7-dehydrocholesterol. Lactic acid is developed by culturing with Streptococcus lactis.

Analysis (submitted by manufacturer).—Moisture 2.65%, ash 4.50%, fat (ether extract) 20.09%, protein (N × 6.38), 20.30%, carbohydrates (by difference) 49.17%, lactic acid 3.29%, iron 0.007%.

Vitamins	*Per Hundred Grams*
Vitamin A	1,325 U.S.P. units
Thiamine	0.21 mg.
Riboflavin	0.46 mg.
Ascorbic acid	8.83 mg.
Vitamin D	350 U.S.P. units

Calories.—4.6 per gram; 130 per ounce.

H. J. Heinz Company, Pittsburgh

HEINZ JUNIOR APPLE SAUCE. Ingredients: Peeled and cored apples (strained), sugar and water as required.

Analysis (submitted by manufacturer).—Total solids 15.78%, total sugar (as sucrose) 11.92%, acidity (as malic) 0.40%, protein (N × 6.25) 0.19%, fat (by acid hydrolysis) 0.33%, crude fiber 0.57%, ash 0.21%, total carbohydrates (by difference) 14.10%.

Vitamins and Minerals	*Per Hundred Grams*
Vitamin A	26.0 I.U.
Thiamine	0.006 mg.
Riboflavin	0.006 mg.
Ascorbic acid	1.50 mg.
Nicotinic acid	0.053 mg.
Calcium	6.00 mg.
Phosphorus	7.80 mg.
Iron	0.35 mg.
Copper	0.06 mg.

Calories.—0.60 per gram; 17 per ounce.

Use.—As a food for older infants as well as for convalescents, the aged and others requiring special diets.

H. J. Heinz Company, Pittsburgh

HEINZ JUNIOR APRICOTS AND APPLE SAUCE. Ingredients: Peeled and cored apples (strained), apricots and sugar.

Analysis (submitted by manufacturer).—Total solids 17.65%, total sugar (as sucrose) 12.16%, acidity (as malic) 0.72%, protein (N × 6.25) 0.56%, fat (by acid hydrolysis) 0.17%, crude fiber 0.63%, ash 0.55%, total carbohydrates (by difference) 15.10%.

Vitamins and Minerals	*Per Hundred Grams*
Vitamin A	3,320 I.U.
Thiamine	0.009 mg.
Riboflavin	0.013 mg.
Ascorbic acid	2.5 mg.
Nicotinic acid	0.358 mg.
Calcium	15.0 mg.
Phosphorus	21.0 mg.
Iron	0.77 mg.
Copper	0.08 mg.
Salt	40.0 mg.

Calories.—0.64 per gram; 18 per ounce.

Use.—As a food for older infants as well as for convalescents, the aged and others requiring special diets.

H. J. Heinz Company, Pittsburgh

HEINZ JUNIOR PEACHES. Ingredients: Peeled, pitted fresh peaches (strained) and sugar.

Analysis (submitted by manufacturer).—Total solids 21.07%, total sugar (as sucrose) 16.26%, acidity (as citric) 0.42%, protein (N × 6.25) 0.56%, fat (by acid hydrolysis) 0.37%, crude fiber 0.47%, ash 0.44%, total carbohydrates (by difference) 18.82%.

Vitamins and Minerals	*Per Hundred Grams*
Vitamin A	315 I.U.
Thiamine	0.007 mg.
Riboflavin	0.018 mg.
Ascorbic acid	0.80 mg.
Nicotinic acid	0.460 mg.
Calcium	11.0 mg.
Phosphorus	17.0 mg.
Iron	0.12 mg.
Copper	0.14 mg.

Calories.—0.81 per gram; 23 per ounce.

Use.—As a food for older infants as well as for convalescents, the aged and others requiring special diets.

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SATURDAY, JANUARY 14, 1950

THE SECOND SESSION OF THE EIGHTY-FIRST CONGRESS

When President Truman addressed the Eighty-First Congress at the opening of its second session he called for, among other things, expansion of hospitals, more doctors, nurses and public health services and the establishment of "a system of medical insurance that will enable all Americans to afford good medical care." While the part of Mr. Truman's message that related to health was comparatively brief, it seemed apparent to most observers that Administration views on expansion of social security and compulsory health taxation programs were not changed from those expressed when this Congress was meeting in its first session.

Various measures were offered to Congress in its first session to advance the "welfare state," but few were passed. However, those concerned with health are of great concern to the medical profession, and physicians should be constantly aware of them and of pending legislation. It was only by last minute, almost heroic efforts that attempts to include physicians under Social Security and to pass Reorganization Plan 1 were thwarted. The defeat of these proposals was important to those who wish to preserve some of the fundamental rights of citizens under the Constitution of the United States, but the defeat was associated with special significance for physicians because they observed how accomplishments can be effected with determination and perseverance.

Many who are familiar with congressional problems are inclined to believe that this second session of the Eighty-First Congress will be much shorter than the first session because of the desire of congressmen to return to their home districts in anticipation of the coming elections and because an election year is not a good year for the proponents of legislation that is generally regarded as highly controversial or socialistic. However, there will be time for much unfinished business, and the medical profession should be alert to what may transpire. Indifference could be costly. Already the federal government has made decisive gains toward the development of a "welfare state." Other proposals are pending, especially those Titles which have passed the Senate and are awaiting action by the House.

The present Congress has considered more bills relating to medical health legislation than any other Congress in the history of the United States. Almost 300 such measures were introduced, but only one bill, S. 614, Amendment to the Hospital Construction Act, was passed in the first session of Congress. The other bills remain on the agenda for the second session. Some of the bills already have been discussed in THE JOURNAL; others will be mentioned as the occasions arise. However, in view of the reconvening of Congress, attention is drawn to pending legislation which is said to be scheduled for early vote. Summaries or more complete information may be obtained from the Washington office of the American Medical Association.

S. 1679 would provide medical care to about 85 per cent of the population through National Compulsory Health Insurance. Wages up to $4,800 annually would be taxed 3 per cent initially, and Treasury funds could be used to meet additional costs. Medical, dental and hospital care would be provided up to 60 days. The bill also would provide federal assistance for medical research and to states for education of health personnel, hospital construction, special aid for rural and other areas with health shortages, local public health units, research in child life and grants for maternal and child health and crippled children's services. There has been opposition to this bill from the American Medical Association. Hearings were held in the Senate and House in the first session of Congress and adjourned indefinitely.

S. 1456 would provide aid to states to assist persons to meet the cost of medical care, including 60 days of hospitalization and outpatient services in hospital or diagnostic clinics. The objectives would be accomplished by encouraging persons to purchase nonprofit, prepayment plans for hospital and medical care. Federal funds would be apportioned to the states to meet matching state funds by which persons not able to afford any or all the cost of such insurance would be subsidized. The bill also provides for surveys of the need for additional diagnostic facilities, domiciliary facilities and of means of attracting practicing physicians to rural areas. Hearings have been held in the Senate and recessed indefinitely. While the subsidizing of states that would administer their own plans is preferable to a straight federal subsidy, the bill as it is written has so many unacceptable provisions that opposition from the American Medical Association is unavoidable.

S. 1581 is concerned with the use of federal funds to assist states in developing programs for health, hospital, medical and dental services for persons unable to pay all costs. It also contains other provisions. S. 1970 would distribute federal funds through state programs to enable persons to purchase voluntary health insurance at rates which they can afford. Other provisions are included. Because of unacceptable provisions in both bills, opposition from the American Medical Association has been presented.

Social Security Legislation (H. R. 6000) was considered by the Board of Trustees at the Washington Clinical Session of the American Medical Association, and the results of the Board's deliberation have been published in an earlier issue of THE JOURNAL.[1] The bills for Federal Aid to Medical Education (S. 1453 and H. R. 5940) were commented on jointly by the Board of Trustees and the Council on Medical Education and Hospitals at the Washington meeting.[2] The School Health Act (S. 1411) also received criticism by the House of Delegates.[2a]

Congressmen already have been advised of these actions. It now remains for physicians to communicate with their senators and representatives. By expressing their opinions, physicians can lend invaluable aid to the efforts of local and state societies and of the national organization opposed to the imposition of the "welfare state" on the people of this country. The members of the House of Delegates were elected by their constituencies to consider medical problems. They have exposed repeatedly the fallacies associated with the development of a "welfare state" and the crippling influences that it would exert on our way of living. If the deliberations and recommendations of the members of the House are to become fully effective, they must be supported by the physicians, who, after all, chose the delegates.

THE ALLEGED SHORTAGE OF PHYSICIANS

During the past few years officials of the Federal Security Agency frequently have alluded to a shortage of physicians which will exist, they claim, in 1960 if heroic measures are not taken to increase enrolments in medical schools. The Federal Security Agency recently published a bulletin entitled "Health Service Areas: Estimates of Future Physician Requirements," by Mountin, Pennell and Berger.[1] This 89 page study is intended to reveal the number of physicians needed in 1960 to meet certain "minimum measures of adequacy." The base year from which the compilations are projected is 1940. The authors have estimated that there will be 227,000 physicians living in the United States in 1960 and that this will provide 143 physicians per 100,000 population. In 1940 there were 133 physicians per 100,000 population. Thus, the first conclusion of the authors is that the number of physicians per 100,000 population will rise from 133 to 143 between 1940 and 1960. The medical population has increased more rapidly than the general population since 1940, and the authors offer assurance that this trend will continue until 1960.

The data offered in the Federal Security Agency report can be questioned on several counts. For example, in one table figures are presented that show the number of physicians per 100,000 population has declined from 149 in 1909 to 125 in 1929; thereafter the number rose to 133 in 1940 and to 137 in 1949. This compilation does not take into consideration, however, the fact that the earlier decrease in the physician-population ratio was the result of the closing of weak medical schools and "diploma mills." The significance of the term "physician" with respect to training and ability differs so markedly today from the significance of the term in 1909 that any crude statistical formula invoked to compare or contrast the situation in the two periods must be rejected. It is interesting to observe that, although the authors have included this table in their bulletin, they do not utilize it in deriving their "minimum measures of adequacy." There are reasons to believe that there will be several thousand more physicians in the United States in 1960 than the 227,000 estimated in this study. Nevertheless, it is reassuring to know that even the authors of this study predict that the number of physicians per 100,000 population will increase. The United States already has the largest number of physicians per 100,000 of any nation except Palestine, where there is a large number of refugee doctors.

Mountin, Pennell and Berger do not accept 143 physicians per 100,000 population as adequate for 1960. In estimating the "adequate" number for 1960, the authors begin with the active nonfederal physicians in 1940 in each of 126 politically boundaried health service regions; they then array these regions in descending order of number of physicians per 100,000 population and then select the twelfth, sixteenth and thirty-seventh regions as standards A, B and C. (The final estimates for 1960, however, include all physicians alive in 1960 rather than just the active nonfederal physicians.) Under method A the twelfth region, the center of which is Buffalo, is set as the standard because one fourth of the population of the United States in 1940 lived in the first twelve regions. Since the Buffalo region contained 146 active nonfederal physicians per 100,000 population in 1940, the authors

1. J. A. M. A. **141**: 1155 (Dec. 17) 1949.

2. (*a*) Footnote 1, J. A. M. A. **141**: 1249 (Dec. 24) 1949. (*b*) Ibid. **141**: 1163 (Dec. 24) 1949.

1. Mountin, J. W.; Pennell, E. H., and Berger, A. G.: Health Service Areas: Estimates of Future Physician Requirements, Federal Security Agency, U. S. Public Health Service, Bulletin 305, 1949.

reason that the 114 regions which had fewer than this ratio should be brought up to the level of 146 by 1960 while the regions 1 to 12 are left with their 1940 ratios. The center of the sixteenth region is Newark, N. J. This region is chosen as the standard under method B because one third of the people in 1940 lived in the first sixteen regions. The authors propose under method B to increase by 1960 the supply of physicians sufficiently to raise the 110 regions below the Newark level up to the Newark level of 136 and to maintain the 1940 ratios in regions 1 to 16. Likewise they select region number 37, the center of which is Madison, Wis., as their standard under method C because one half of the people of the United States in 1940 lived in these first 37 regions. On this basis they would recommend increasing the medical population to provide the Madison level of 118 active nonfederal physicians per 100,000 population in all the 89 regions below this level while maintaining the 1940 ratios in regions 1 to 37. Translated into national ratios for all physicians, not just active nonfederal, method A assumes that the physician-population ratio in 1960 should be 172, method B, 165 and method C, 154, instead of the 143 which the authors predict. The 1960 deficits according to the three "minimum measures of adequacy" will be 45,053, 33,666 and 17,413. Instead of the 227,119 physicians predicted for 1960, under these three estimates there should be 272,172, 260,785 and 244,532.

The methods employed in this study are so unrealistic that the study adds nothing to the knowledge of the physician requirements of the American people now or in 1960. The authors have not made any apparent attempt to rate these 126 health service regions according to mortality and morbidity rates, in spite of the fact that the 1940 crude death rate (unadjusted for age distribution) was roughly 11.8 deaths per 1,000 population for the top 12 regions in the authors' array according to number of physicians per 100,000 population and only 10.2 in the lowest twelve of the 126 regions. Furthermore, the Buffalo region, the first standard used, contains two medical schools. The inference from method A is, therefore, that every one of the 114 health service regions below the Buffalo level should contain the equivalent of two medical schools. In addition, the Buffalo ratio of 146 set as the standard under method A would be reduced to 135 if the interns, residents and the teachers in that region were eliminated and would be further reduced if the physicians employed by industry also were eliminated. Although the Newark region does not have a medical school, the number of interns, residents and industrial physicians is too large to permit use of the Newark region as a standard. The Madison region does have a medical school.

The authors do not claim that the additional physicians needed in 1960 as computed by methods A, B and C would, if available, actually practice medicine in those regions below the three selected regions in the array of 126 regions. Apparently they are attempting to determine only the over-all national deficit. The authors make it clear that these calculated deficits existed in 1940 and are not deficits which will arise between 1940 and 1960. If their three calculated deficits for 1940 were adjusted upward to allow for inactive and federal physicians, the shortages under their three methods for 1940 would actually exceed their shortages for 1960. Thus it is obvious that these shortages for 1940 or 1960 are declared shortages or assumed shortages. The methods employed by the authors established the shortages; an attempt is not made in this particular study to prove or disprove that there was a shortage in 1940. Had the number of physicians in each of the 126 regions been twice as great in 1940, their deficits would likewise have been twice as great. Their study provides an excellent example of an assumed conclusion.

If a method of measuring national shortages of physicians is valid, it should be equally applicable to most, if not all, professions and occupations. It could be shown by the authors' methods that in 1940 there was an inadequate number of dentists, of teachers, of lawyers and of persons in every gainfully employed occupation. In fact, one might deduce the principal fault with the United States was that there were only 132,000,000 persons in 1940 when actually the authors' "minimum measures of adequacy" would have required forty or fifty million additional!

It is difficult to forecast the national demand for physicians because it is practically impossible to estimate in advance the rapidity of technologic progress in the practice of medicine. Nevertheless, it is possible that there will be a surplus of physicians in 1960. During the 1940's a great increase in the number of auxiliary personnel, as well as improvements in therapeutic remedies, greatly enhanced the amount of medical service which any 1,000 physicians could render. The Bureau of Medical Economic Research of the American Medical Association has estimated that the increase in productivity per physician during the 1940's might have been as much as one third. If this rapid and widely recognized trend continues, it certainly seems more reasonable to expect a surplus than a deficit of physicians in 1960. Obviously a crisis in the health of the people does not now exist. In any event, physician-population ratios are not true measures of the demand or supply of physicians. The most important objective is raising the standards of performance in the medical profession. The number of physicians divided by

the number of people and multiplied by 100,000 to obtain the ratio of physicians per 100,000 population certainly cannot be expected to provide a satisfactory guide to Congress or to the American people on the number of physicians needed. A satisfactory study would pinpoint the situation in every section of the United States.

Mountin, Pennell and Berger appear to have arbitrarily chosen 1960 as the year when the number of physicians in the low ratio areas of 1940 should meet their three arbitrarily chosen "minimum measures of adequacy." Why not take 1970 or 1980 as the objective? In fact, even the data furnished by the authors suggest that by 1980 the steady increase in the number of physicians per 100,000 population will meet standards B and C and possibly standard A set by the authors. The arbitrary selection of 1960 as a goal supports the impression that the authors have "assumed their conclusions."

Current Comment

ASSOCIATION OF INTERNS AND MEDICAL STUDENTS

The delegates of the Association of Interns and Medical Students at their recent annual convention in Chicago are reported to have supported a prepaid national government-sponsored health program as the "best method that has been proposed for providing adequate medical care for the largest number of people in the country and adequate remuneration for services of the doctor." The delegates of this organization, which has been accused of Communistic affiliations, also are reported to have favored federal aid to medical education, improved working conditions for interns with vacations, time off, monthly salaries of $100 and no discrimination. They appear to believe that assistant resident physicians should receive $150 and resident physicians $200 per month, with provisions for accident insurance and special compensation for ambulance work, which they apparently regard as sufficiently hazardous to justify special financial recognition. The delegates voted to end their affiliation with the International Union of Students, which is said to be Communist dominated; in spite of this claim of disaffiliation, they decided to cooperate with the International Union of Students in the exchange of students. Many of the medical students, interns and resident physicians who are members of the Association of Interns and Medical Students probably are well meaning persons, but their membership in an organization which cooperated with the International Union of Students will leave their sincerity and loyalty open to question by discerning critics. They would do well to examine carefully the activities of any organization that they may be invited to join. Otherwise, they may risk considerable embarrassment.

SALIVARY TASTE HORMONES

Phenylthiocarbamide (PTC) tastes bitter to 60 per cent of all Caucasians. The remaining 40 per cent find it tasteless. To explain this hereditary taste blindness, it was suggested by Blakeslee,[1] Fox [2] and others that the saliva of those who cannot taste the chemical presumably contains a precipitant which renders the phenylthiocarbamide nonstimulating to the taste buds. This hypothesis has been studied by Cohen [3] and his associates of the Department of Psychology, University of Illinois. Thirty-five college students were first tested with phenylthiocarbamide crystals and each subject classified as a "taster" or "nontaster." Then each subject was retested with (*a*) a saturated solution of phenylthiocarbamide in tap water on a tongue dried by an atomizer, (*b*) a saturated solution of phenylthiocarbamide in nontaster saliva on a dry tongue, (*c*) a saturated solution of phenylthiocarbamide in alien taster saliva and (*d*) a saturated solution of phenylthiocarbamide to the subject's own taster saliva. Data thus obtained indicate that a person will taste phenylthiocarbamide as bitter when he has the one necessary anatomic "taste apparatus" supplemented by his own saliva; phenylthiocarbamide cannot be tasted when the crystals are dissolved in water and saliva is not used; a nontaster cannot taste phenylthiocarbamide even when he uses taster saliva, and a taster cannot taste phenylthiocarbamide when he uses nontaster saliva or the saliva of another taster, his own saliva being essential. Thus there apparently is not a phenylthiocarbamide precipitant in nontaster saliva, but an individual phenylthiocarbamide taste activator in the subject's own saliva. To test whether a similar activator is necessary with other substances, the same tests were made with saturated aqueous solutions of saccharin and sodium chloride. All students were able to taste saccharin and salt on a wet tongue, but 16 failed to detect saccharin and 9 could not taste sodium chloride on a dry tongue. The conclusion was drawn that a person's own saliva contains numerous specific taste activators, a conclusion of considerable clinical interest. The chemical nature of these salivary taste hormones is now under investigation.

PUBLIC PAYROLL IN GREAT BRITAIN

According to a recent report in the press, more than one tenth of the population in Great Britain is on the public payroll. The Minister of Labor is reported to have said that the employees of nationalized industries and other public services number 2,500,000. This number and that for other employees on the public payroll total 5,700,000 of a total population of about 50,000,000. What will happen if every activity is nationalized and everyone goes on the public payroll? Who will pay the toll?

1. Blakes'ee, A. F.: Science **74**: 607, 1931.
2. Fox, A. L.: Proc. Nat. Acad. Science **18**: 115, 1932.
3. Cohen, J., and Ogdon, D. P.: Science **110**: 532, 1949.

ORGANIZATION SECTION

Official Notes

DR. HALL APPOINTED SECRETARY OF COUNCIL

The Board of Trustees has appointed Dr. Robert M. Hall as Secretary of the Council on National Emergency Medical Service effective January 1. Dr. Hall, who was born in Nebraska in 1917, graduated from Dartmouth College in 1939 and Harvard Medical School in 1943. He served an internship in medicine at Roosevelt Hospital, New York, and as an assistant resident in medicine at Duke Hospital, Durham, N. C. He was a battalion and regimental surgeon with the Second Infantry Division during World War II and from December 1948 to December 1949 was with the Research and Development Board in the Surgeon General's office.

Washington Letter

(From a Special Correspondent)

Jan. 9, 1950.

Instruction on Hazards of Atomic Warfare

Three federal agencies are co-sponsoring a new training program, the purpose of which is to develop appreciable numbers of instructors in medical hazards of atomic warfare. Through a series of one week teacher-training courses, selected members of the medical profession will be equipped to relay acquired information to physicians, dentists, nurses and other health scientists in their local communities. Sponsoring the project are the U. S. Atomic Energy Commission, National Security Resources Board and General Services Administration. The courses will be inaugurated in March at Argonne National Laboratory, Chicago; the Atomic Energy Project at University of Rochester, and Western Reserve University School of Medicine, Cleveland. Institutions where the training will be given later in the spring include University of California at Los Angeles, University of Utah School of Medicine, University of Alabama School of Medicine and Johns Hopkins School of Medicine. Trainees, in the main, will be representatives of medical societies, medical schools and state and municipal governments. Invitations to make nominations will be issued by the National Security Resources Board. Plans for the instruction program were made late in December by a group comprising Drs. Shields Warren, Charles L. Dunham and John Z. Bowers, Atomic Energy Commission; Norvin C. Kiefer, National Security Resources Board; Henry A. Blair, University of Rochester; Austin M. Brues, Argonne National Laboratory; Hymer I. Friedell, Western Reserve University; B. V. Jager, University of Utah; Perrin H. Long, Johns Hopkins University, and William H. Riser Jr., University of Alabama.

Neglect of Mentally Ill Veterans

A recent statement by Veterans Administration that recovery of many mentally ill veterans is being retarded by failure of families and friends to visit them has been criticized as "misleading" by Veterans of Foreign Wars. George E. Ijams, rehabilitation director of VFW, accused the government agency of being derelict in its responsibilities to the same veterans through delay or failure in pressing their compensation claims.

"While it is true," he said, "that the welfare and progress of many of these veterans will be affected by the interest and concern shown by their families, it is equally true that prompt action by VA to grant many of our mentally helpless veterans the compensation and other benefits to which they are entitled will contribute just as much to their present well-being and eventual recovery."

Stating that VA's responsibilities to mentally ill beneficiaries are not limited to hospitalization and medical care, Ijams said, "The law clearly provides that those suffering mental disabilities resulting from military service or who have received physical disabilities while under the care and supervision of VA for mental illnesses are entitled to compensation. The failure of hospital officials to file official claims for these veterans within the required period of time does not relieve VA of this responsibility and, most certainly, does not void the entitlement of these veterans to these benefits."

Nine Volumes of Nuclear Energy Series in Use

Nine volumes, totaling 5,428 pages, in the National Nuclear Energy Series of monographs on wartime and postwar research have been published to date by the Atomic Energy Commission. Describing achievements in medicine, biology, chemistry and other fields, the series is expected to cover 50 or more volumes. It was inaugurated in December 1948 by "Histopathology of Irradiation from External and Internal Sources," by William Bloom, M.D. The second volume to be published was "Pharmacology and Toxicology of Uranium Compounds," by Carl Voegtlin and Harold C. Hodge, which summarizes three years of study on toxicity of uranium compounds and the mechanism of uranium poisoning.

Streptomycin Manufacture Abroad Facilitated

An industrial guaranty contract was signed in December by the Heyden Chemical Corp., New York City, and the Export-Import Bank of Washington, the latter acting as agent for the Economic Cooperation Administration, the objective of which is to facilitate manufacture of streptomycin in France. First to be issued by ECA for an industrial investment in France, the guaranty provides that receipts on the Heyden firm's investment may be converted into dollars. The company plans an investment of at least $100,000 and the guaranty is for $175,000, covering capital outlay of $100,000 and an earnings increment of $75,000. During its first year of operation, ECA financed $6,000,000 worth of streptomycin for French use.

Subtilin Effective as Food Preservative

Successful use of the antibiotic subtilin as a bactericidal agent in the process of canning vegetables has been reported by U. S. Department of Agriculture. G. E. Hilbert, chief of the Bureau of Agricultural and Industrial Chemistry, cautioned that the technic is stil experimental and that "one particularly important question—whether the antibiotics, as used, are toxic to man—can be answered only after long and careful investigation." Results to date indicate that addition of subtilin permits sterilizing of the cans with heat more rapidly, at lower temperatures and without pressure-cooking equipment.

Bids Solicited for Veterans Hospital at Boston

The Army Engineers Corps announced December 29 that bids for construction of a 1,000 bed Veterans Administration hospital at Boston will be accepted until Feb. 7, 1950. They will be opened on that date at the New England Division Engineers Office in Boston.

Coming Medical Meetings

Annual Congress on Medical Education and Licensure, Chicago, Palmer House, Feb. 5-7. Dr. Donald G. Anderson, 535 N. Dearborn. St., Chicago, Secretary.

National Conference on Rural Health, Kansas City, Mo. Feb. 3-4. Dr. F. S. Crockett, 535 N. Dearborn St., Chicago, Chairman.

American Academy of Orthopedic Surgeons, New York, Waldorf-Astoria Hotel, Feb. 11-16. Dr. Harold B. Boyd, 869 Madison Ave., Memphis, Tenn., Secretary.

GOVERNMENT SERVICES

ARMY

PRIZE-WINNING EXHIBIT

The exhibit "Tumors of the Lung" and "Cancer Cells in Sputum and Bronchial Secretions," which won a prize at the American Medical Association's annual meeting in Atlantic City last June, has been loaned to the Armed Forces Institute of Pathology, Washington, D. C., by the Mayo Foundation and is now on exhibition at the Army Medical Museum. Prepared by Drs. J. R. McDonald, L. B. Woolner and C. Allen Good, under the technical supervision of Dr. Arthur H. Bulbulian, director of the Museum of Medicine and Hygiene, Mayo Foundation, Rochester, Minn., the exhibit is based on experience with tumors of the lung as seen in the surgical pathology laboratory. It includes data on bronchogenic carcinoma, bronchial adenoma, pulmonary adenomatosis and other neoplastic conditions of the lungs; also shown is the cytologic examination of sputum and bronchial secretions as an aid in the diagnosis of bronchogenic carcinoma. The exhibit will be on display until April 22, 1950.

MONTHLY MEDICAL MEETING

The regular Surgeon General's monthly medical meeting at the Army Medical Center, Washington, D. C., Dec. 15, 1949, was addressed by Dr. Isadore S. Ravdin of Philadelphia, on "Carcinoma of the Large Bowel."

COLONEL COX HONORED

In recognition of the best paper presented before the First Inter-American Congress on Industrial Hygiene in Buenos Aires, Dec. 14, 1949, Col. Wesley C. Cox (MC), chief of the Army Industrial Hygiene Laboratory, received a gold medal. The presentation was made by the president of the Argentine Republic, Gen. Juan Peron. In his paper Colonel Cox traced the development of governmental industrial hygiene in the United States from about 1912 until the recent national emergency.

CERTIFIED BY SPECIALTY BOARDS

The following Army medical officers have recently been certified by American Specialty Boards:

Col Albert R. Dreisbach, preventive medicine and public health.
Col. Robert P. Rea, otolaryngology.
Col. Charles T. Young, internal medicine.
Lieut. Col. Robert L. Cavenaugh, pathology.
Lieut. Col. Joseph B. Gordon, general surgery.
Lieut. Col. John H. Kuitert, physical medicine.
Lieut. Col. Arthur P. Long, preventive medicine and public health.
Lieut. Col. Myles P. Moursund, dermatology and syphilology.
Lieut. Col. O. Elliott Ursin, preventive medicine and public health.
Major Abraham Chartock, radiology.
Major Nelson S. Irey, pathology.

VETERANS ADMINISTRATION

RESIDENCIES IN NEUROPSYCHIATRY

A limited number of openings are available for July 1, 1950 appointment to the Veterans Administration residency training program in neuropsychiatry. This program is under the jurisdiction of the deans of the Boston medical schools (Harvard, Tufts, Boston University). The training, which may be from one to three years, is given at:

Cushing Veterans Administration Hospital, Framingham, Mass.

Bedford Veterans Administration Hospital, Bedford, Mass.

The Mental Hygiene Clinic of Boston, Regional Office of Veterans Administration, Boston.

West Roxbury Veterans Administration Hospital, West Roxbury, Mass.

White River Junction Veterans Administration Hospital, White River Junction, Vt.

Training in child psychiatry is given at Childrens Center, Massachusetts General Hospital and Habit Clinic, all in Boston. For information write to: Dr. J. L. Hoffman, Chief, Professional Services, Bedford Veterans Administration Hospital, Bedford, Mass.

PERSONAL

Dr. Bruno G. Schutkeker has been appointed chief of neuropsychiatry at the new Veterans Hospital in Buffalo. Dr. Schutkeker is a native of Buffalo, a graduate of the University of Buffalo Medical School, veteran of World War II, Surgeon General of the New York National Guard and a specialist certified by the American Board of Neuropsychiatry.

Dr. Cleve C. Odom has resigned as manager of the Veterans Administration's Lenwood Hospital at Augusta, Ga., to become superintendent of the South Carolina State Hospital and director of the South Carolina state mental hygiene activity. His successor will be Dr. Lee R. Tighe, who has been chief of professional services, Veterans Hospital, Murfreesboro, Tenn.

PUBLIC HEALTH SERVICE

PROBLEMS WHICH CONFRONT NEW HOSPITALS

A conference on problems which confront new hospitals was held in Atlanta, Ga., Nov. 15-17, 1949. The conference was sponsored by six Southeastern states in cooperation with the Division of Medical and Hospital Resources of the Public Health Service. The sponsoring states were Georgia, South Carolina, Tennessee, Alabama, Florida and Mississippi. The purpose of the meetings was to acquaint state agency personnel with the tasks confronting any hospital approaching the day when the first patients will be admitted. The meetings were open to administrators and trustees of new hospitals in the southeastern region. Forty persons representing new hospitals were among the 85 in attendance. Papers presented included: "Personnel Problems, Policies and Sources," by H. Carl Rowland, assistant administrator, Spartanburg General Hospital, Spartanburg, S. C.; "Legal Aspects of Hospital Operation," by R. F. Whitaker, superintendent, Emory University Hospital, Emory University, Georgia, and "The Hospital Administrator," by Marshall I. Pickens, the Duke Endowment, Charlotte, N. C.

Dr. John R. McGibony, chief of the Division of Medical and Hospital Resources, stated that this conference might be a prelude to similar sessions in other parts of the country, as hundreds of new hospitals will be opened during the next few years under the National Hospital Program.

NATIONAL ADVISORY CANCER COUNCIL

Two new members have been appointed to the National Advisory Cancer Council: Dr. William U. Gardner, professor of anatomy at Yale University, and Dr. Paul E. Steiner, professor of pathology at the University of Chicago. They replace Dr. Shields Warren of the New England Deaconess Hospital, Boston, and Dr. Waltman Walters of the Mayo Clinic, whose appointments to the Council expired January 1. The next meeting of the council will be in February.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

ARIZONA

Sanitation Code for Schools.—The Arizona State Board of Health at its November meeting adopted a school sanitation code. For the first time in the state all plans for the construction of new school buildings and additions to existing buildings must be approved by the state department of health to meet minimum standards in ventilation, heating, lighting, water supplies, drinking fountains and school lunch room facilities. School grounds as well as structures must meet certain specifications.

GEORGIA

Society News.—At the November meeting of the Atlanta Eye, Ear, Nose and Throat Society the following officers were elected: Dr. Lester A. Brown, president, Dr. William T. Edwards Jr. vice president and Dr. James T. King secretary-treasurer.

Dr. Calhoun Heads Department of Ophthalmology.—Dr. F. Phinizy Calhoun Jr., instructor in ocular pathology, Emory University School of Medicine, Atlanta, has been promoted to professor and chairman of the department of ophthalmology. Dr. Calhoun received his M.D. degree from Johns Hopkins University School of Medicine, Baltimore, in 1936. He served a residency at the Institute of Ophthalmology, Presbyterian Hospital, Columbia University, New York, 1939-1942, and was in the Army medical corps, 1942-1945. Dr. Alton V. Hallum, assistant professor of ophthalmology at the university has been promoted to professor of clinical ophthalmology. Dr. Hallum has been on the staff since his graduation from the university in 1929.

ILLINOIS

State Health Department Report.—Summarizing the activities of the state department of public health, Dr. Ronald R. Cross, director, termed the year 1949 outstanding in accomplishments. "In addition to our long-established services, several new and essential programs have been inaugurated and other functions advanced to the organizational stage," he said. "Favorable legislation has permitted us to extend our activities in many important fields. An extension of state aid for local hospitals, the separate appropriation for state tuberculosis hospital construction, strengthening of the sanitary water board's powers and needed changes in the law concerning local referendums on county health department formation have materially aided our program." He said that in 1949 Illinois put into operation the most widespread tooth-saving program of any state in the nation. The health department's dental x-ray service has been expanded to provide more than 100,000 x-rays yearly. Four teams of dental experts will have completed about 35,000 applications of decay-preventing sodium fluoride to the teeth of Illinois school children by the end of the 1949-1950 school year. Under a newly organized program of diagnosis and treatment of heart diseases, begun in July 1949, four projects, located in Springfield, Rockford, East St. Louis and Savanna, are already functioning. The growing program of study and treatment of mental diseases has also been intensified. The state's tuberculosis case-finding program, carried on primarily through the use of x-ray units traveling from community to community, was of service to some 280,000 Illinois citizens during 1949. "It is largely due to this extensive tuberculosis case-finding program that Illinois' reported cases of tuberculosis have risen slightly this year." Dr. Cross said. Three new cancer clinics were opened, bringing the total of such diagnostic centers to 24 within the state, operating with the assistance of the state department of public health. In these clinics 4,150 patients were given first examinations in 1949; 4,802 received follow-up examinations, and tissue examinations for 3,763 indigent patients were made.

Chicago

Changes in Faculty at Chicago University.—One hundred and fifty friends and colleagues of Dr. Oswald H. Robertson, professor of medicine, met at the Quadrangle Club on the university's campus recently for a dinner on the occasion of Dr. Robertson's retirement from the university after 22 years of active service. Dr. Robertson has accepted an appointment at Stanford University continuing his ecological investigations. Leonidas Marinelli has been appointed to the staff of the School of Medicine. He holds the title of research associate with the rank of assistant professor. Mr. Marinelli is also on the staff of the Argonne National Laboratory.

Society News.—The Chicago Medical Society will hold a meeting at the John B. Murphy Memorial Auditorium on January 18 at 8 p. m. Dr. Cornelius P. Rhoads, New York, will speak on "Recent Developments in the Treatment of Cancer," and Dr. Jerome W. Conn, Ann Arbor, Mich., on "Experimental Work in Diabetes with Pituitary Adrenal Corticotropic Hormone (ACTH)." A dinner in honor of the guest speakers will be held at the Drake Hotel at 5:30 p. m. For reservations call the society office, Central 6-3026.

New Teaching Hospital at Illinois.—Construction of a 14 story addition to the Research and Educational Hospitals of the University of Illinois has begun. Erection of the 411 bed teaching hospital represents one of the largest construction projects in the history of the university; contracts alone total $5,368,628. The building is expected to be completed within 18 months. The addition to the hospital will raise the amount of present construction in the Medical Center District to more than $25,000.000. Other projects now under construction are the Veterans Administration Hospital, the Chicago State Tuberculosis Hospital, Cook County Interns' Residence and the Nurses' Residence at Presbyterian Hospital. The hospital addition will enable the university to handle its clinic patients more efficiently. More than 7,000 patients received bed treatment at the Research and Educational Hospitals during the past fiscal year, while an additional 189,000 visits were handled in the 24 outpatient clinics. The addition is the first of two major buildings needed to add 24 new students to each class now numbering 166 in the College of Medicine. The hospital addition will also enable the university to expand its medical research activities.

The entire first floor and about one third of the second, third and fourth floors will be devoted to outpatient services. The lower floors also will contain the department of radiology, which will render both diagnostic and therapeutic services, a central diagnostic laboratory, including a blood bank, a dispensing and manufacturing pharmacy, the main kitchen and dining room and a unit where all hospital records will be filed. Occupational and physical therapy will be available for all patients, and teaching of therapists will be carried on. The new addition will contain 14 operating rooms, two delivery rooms, a premature nursery, housing for interns and an emergency station containing two operating rooms and an x-ray and fracture room in the basement.

INDIANA

State Society Organizes Grievance Committee.—The Indiana State Medical Association has announced the organization of a grievance committee, composed of five of its past presidents. The following members have been appointed: Drs. Jacob T. Oliphant of Farmersburg, chairman; Carl H. McCaskey of Indianapolis, Augustus P. Hauss of New Albany, Charles N. Combs of Terre Haute and George R. Daniels of Marion. The committee will collect evidence as would a grand jury, and, when it believes a physician is guilty of unethical conduct, the case will be referred to his county medical society or to the council of the state association for appropriate action. Only complaints made in writing will be considered. A copy of the complaint will be forwarded to the physician involved with a request that he contact the patient and try to reach a satisfactory understanding. Later, if necessary, the principals will be invited to appear before the committee and submit evidence. Dr. Oliphant pointed out that, because of the assistance of the state medical association, doctors are now available for emergencies on a round-the-clock basis in all Indiana communities through arrangements made by the county medical societies. Most county societies have boards of censors or ethics committees to which are referred complaints against local doctors, but the profession thinks a grievance committee at the state level will be more effective. Complaints may be sent to members of the grievance committee or to the Indiana State Medical Association, 1021 Hume Mansur Building, Indianapolis 4.

LOUISIANA

Dr. Blalock Awarded the Matas Medal.—Dr. Alfred Blalock, Baltimore, originator of the "blue baby" operation, will receive the Rudolph Matas Award in Vascular Surgery January 17 at 8:30 p. m. in the Hutchinson Memorial Building of Tulane University of Louisiana School of Medicine, New Orleans. The award was established in honor of Dr. Rudolph Matas, emeritus professor and former head of the department of surgery at Tulane and pioneer in vascular surgery. Dr.

Matas, now 89 years old, will present the medal to Dr. Blalock. Dr. Rufus C. Harris, president of Tulane, will preside. Dr. Blalock is director of the department of surgery at Johns Hopkins University School of Medicine. The "blue baby" operation, which was first performed on November 29, 1944, is designed to correct a congenital interference with an adequate supply of oxygenated blood. Dr. Blalock devised an operation in which an anastomosis is made between a branch of the aorta and one of the pulmonary arteries.

The Matas award was founded in 1934, when the family of Miss Violet Ida Hart established a fund to finance an award "to the North American surgeon who has contributed outstanding work in vascular surgery." The following permanent committee of New Orleans surgeons was named to select the recipients of the award: Drs. Emile Bloch, chairman; Isidore Cohn, Lucian Landry and Alton Ochsner. The previous recipients of the award were Dr. Mont R. Reid, late professor of surgery, University of Cincinnati; Dr. Reynaldo dos Santos of Lisbon, Portugal; Dr. Daniel Elkin, professor of surgery, Emory University, Atlanta, Ga., and Dr. Robert E. Gross, William E. Ladd professor of children's surgery, Harvard University, Boston. In the case of Dr. dos Santos, the committee members obtained permission of the Hart family to waive the stipulation limiting the award to a North American. Dr. Blalock received his M.D. from Johns Hopkins University School of Medicine in 1922 and returned to his alma mater in 1941 to head the department of surgery and become surgeon-in-chief of Johns Hopkins Hospital. Much of the basis for Dr. Blalock's surgery has been furnished by the clinical observations of Dr. Helen Taussig, associate professor of pediatrics at Johns Hopkins. In 1948 Dr. Blalock and Dr. Taussig jointly received the Passano Award for outstanding contributions to the progress of medical science.

MARYLAND

Memorial Lectures in Obstetrics.—Doctors Hospital of Baltimore has announced a course of lectures in obstetrics for the general practitioner in memory of Dr. M. Alexander Novey, late director of maternal hygiene, Baltimore City Health Department. The series will consist of 13 lectures at weekly intervals, beginning January 11 and extending through April 5. The lectures are to be held at Doctors Hospital, 2724 North Charles Street, and will be given Wednesday afternoons at 3 p. m. by Baltimore physicians. The series will be opened by Dr. Louis H. Douglass, professor of obstetrics, University of Maryland School of Medicine and College of Physicians and Surgeons, and close friend and associate of Dr. Novey. The program follows:

Jan. 11, Dr. Douglass, Introductory; Maternal Mortality and Morbidity; Essentials of Prenatal Care; Role of the General Practitioner.
Jan. 18, John E. Savage, Toxemias of Pregnancy.
Jan. 25, Nicholson J. Eastman, Special Problems; Age, Parity, Diabetes, Previous Cesarean Section.
Feb. 1, D. Frank Kaltreider Jr., Conduct of the First and Second Stages of Labor; Breech Presentation.
Feb. 8, Robert A. Hingson, Pain Relief and Anesthesia.
Feb. 15, Eleanor Delfs, Bony Pelvis, Pelvimetry; Contracted Pelvis.
Feb. 22, Dr. Douglas, Prolonged and Complicated Labor; Conservatism in Obstetrical Management; Use and Abuse of Pituitary Extracts.
March 1, Louis M. Hellman, Conduct of the Third Stage and Its Complications.
March 8, Alan F. Guttmacher, Hemorrhages of Pregnancy; Multiple Pregnancy.
March 15, Milton S. Sacks, RH Factor and the Blood of the Pregnant Patient.
March 22, George Anderson, Pathology of the Newborn.
March 29, A. Harry Finkelstein, Immediate Care of the Newborn and the Special Problem of the Premature Infant.
April 5, John McF. Bergland, Obstetrics in Retrospect and the Future.

MISSOURI

Hodgen Lecture.—The Hodgen Lecture of the St. Louis Surgical Society will be presented by Dr. Samuel C. Harvey, professor of surgery at Yale University School of Medicine, New Haven, Conn., January 17 on "Reaction to Injury as Exemplified by the Wound—The Regenerative Phase."

NEW YORK

Chest X-Rays for State Employees.—The State Department of Health will begin a mass chest x-ray program of about 40,000 state employees January 17, the first such service since 1946. The survey will be conducted on a voluntary basis.

Postgraduate Lectures.—The following postgraduate lectures have been arranged by the Medical Society of the State of New York with the cooperation of the New York State Department of Health: The Geneva Academy of Medicine and the Geneva Dental Society, meeting at the Bellhurst Restaurant in Geneva January 16 at 8:30 p. m., will hear Dr. Edward G. Schweinberger, Syracuse, speak on "Cleft Palate and Harelip." Dr. James J. Smith, New York, will address the Jefferson County Medical Society on "Alcoholism as a Medical Problem" when it meets at the Black River Valley Club in Watertown January 17 at 6:30 p. m. On January 19 at 9 p. m. the Warren County Medical Society will hear Dr. Edward Sharkey, Albany, speak on "Use of Radioactive Isotopes in Tumor Localization" at the Queensbury Hotel, Glen Falls. "Fluid and Electrolyte Balance" will be the subject of a lecture by Dr. George F. McInnes, New York, at the Hotel Utica January 19 at 8 p. m. before members of the Utica Academy of Medicine. Also on January 19 the Clinton County Medical Society, meeting at 8:15 p. m. at the Champlain Valley Hospital Nurses Home in Plattsburg, will hear Dr. Leon G. Berman, Syracuse, speak on "Diagnosis and Treatment of the Acute Abdomen."

New York City

Miller Fellowship in Tuberculosis Research.—The New York Tuberculosis and Health Association announces that its newly established James Alexander Miller Fellowship for Research in Tuberculosis will be available from July 1, 1950 to June 30, 1951. The fellowship is designed to support a qualified medical investigator who will devote full time to a research project with a definite bearing on tuberculosis. The stipend will be $5,000. Application forms will be supplied on request to the New York Tuberculosis and Health Association, 386 Fourth Avenue, New York 16, and must be submitted in duplicate not later than March 1. Announcement of the award will be made in April.

Dr. Calderone Appointed Director of the Cancer Committee.—Dr. Frank A. Calderone assumed duties January 1 as executive director of the New York City Cancer Committee. Dr. Calderone has resigned from the World Health Organization effective January 1, but will continue as a consultant of the Medical Services of the United Nations. He is a graduate of the New York University Medical School and received his M.P.H. degree from the Johns Hopkins University School of Hygiene and Public Health, Baltimore. He joined the New York City Health Department in 1938, was named secretary of the department of health in 1942, later became deputy commissioner of health and during 1943 and 1945 was acting commissioner of health for extended periods. He joined the staff of the World Health Organization's Interim Commission as director of the New York Headquarters Office in 1946.

OHIO

Lecture on Treatment of Cirrhosis.—Dr. Arthur J. Patek Jr., assistant clinical professor of medicine, Columbia University College of Physicians and Surgeons, New York, will speak at Mount Sinai Hospital of Cleveland January 26 at 8:30 p. m. on "Pathogenesis and Treatment of Laennic's Cirrhosis." Dr. Patek will also hold a clinic January 26 at 10:30 a. m.

Cincinnati General Physicians' Fund.—For three years the Cincinnati Society of General Physicians, in collaboration with the University of Cincinnati College of Medicine, has conducted continuation courses for practicing general physicians. Seventy-five per cent of the small fee that is charged by the society for registration in the postgraduate courses is donated to the College of Medicine in a fund known as the Fund of the Society of General Physicians. The amount contributed since 1947 is $9,715, which is disbursed at the discretion of the dean for the advancement of the work of the college. Since the inauguration of the program 176 hours of lectures have been made available to 812 physicians.

OKLAHOMA

Personals.—Dr. William A. Tolleson, Eufaula, has been awarded the medal of merit by the Department of the Interior for outstanding service over a long period of time in government Indian service.——Dr. David W. Griffin in October completed 50 years of service at the Central Oklahoma State Hospital in Norman, where he has been medical superintendent.

Two County Societies Unite.—The Garfield County Medical Society and the Kingfisher County Medical Society united December 31 to form a new organization, known as the Garfield-Kingfisher County Medical Society. The amalgamation of the two societies was authorized by the House of Delegates of the Oklahoma State Medical Association.

SOUTH DAKOTA

State Association Officers to Meet.—The second annual meeting of officers, councilors and district officers of the South Dakota State Medical Association will be held at the Marvin Hughitt Hotel, Huron, January 29. Mr. Larry Rember, director of public relations of the American Medical Association, Chicago, will speak on "A Medical Public Relations Program for 1950."

TENNESSEE

Institute of Nuclear Studies Appointments. — Dean Louis A. Pardue, Ph.D., of the University of Kentucky Graduate School, became chairman of the Council of the Oak Ridge Institute of Nuclear Studies on January 1. He succeeds J. Harris Purks Jr., Ph.D., who has resigned from Emory University and the institute council to become associate director of the General Education Board. Paul M. Gross, Ph.D., vice president of Duke University, is president of the institute and Dr. William G. Pollard, executive director, is the chief resident officer.

TEXAS

Seminars on Alimentary Tract Physiology.—Dr. Lathan A. Crandall Jr., director of research of the Miles Laboratories, Elkhart, Ind., will give a series of seminars on the physiology of the alimentary tract at the University of Texas Medical Branch, Galveston, January 24 and 25.

Research on Burns. — Special research laboratories have been provided at the University of Texas Medical Branch, Galveston, for the Division of Plastic and Maxillo-Facial Surgery under the direction of Dr. Truman G. Blocker Jr. Dr. R. I. Stout will be associated with Dr. Blocker in research studies on tissue repair and body fluid control in severe burns.

UTAH

Dr. Spies is New State Health Commissioner. — Dr. John W. Spies, Marshallton, Del., became state health commissioner December 5. Dr. Spies received his M.D. degree from Harvard Medical School, Boston, in 1924. He has been an instructor in surgery at Yale University School of Medicine, New Haven, Conn., was assistant and associate professor of surgery and director of the tumor clinic of Peiping (China) Union Medical College, 1931-1935, director of the Tata Memorial Hospital for Cancer, Bombay, India, 1935-1938, and was professor and dean of the University of Texas Medical Branch, Galveston, 1938-1942.

WASHINGTON

Study of Animal Diseases.—A before and after study of wild life and animal diseases is to be launched in the Columbia River Basin to determine the extent of animal diseases which are transferable to man. The 87,000 acre area in Grant County, the first to be opened by the Grand Coulee Dam development, is the object of this study of an area before land reclamation and irrigation bring about fundamental changes and again after land is settled. The area is expected to be a thickly populated farming region by 1952. Several state and federal agencies are working cooperatively. With knowledge of predevelopment conditions, an accurate check on diseases brought into the area by settlers will be possible. The principal diseases which have been detected in animals in the area are plague, tularemia, Rocky Mountain spotted fever, Western equine encephalomyelitis, Q fever and brucellosis. Dr. Wavelin R. Giedt, epidemiologist of the Washington State Health Department, is chairman of the coordinating committee. C. Wesley Clanton of the state department and Monroe A. Holmes Jr., D.V.M., Berkeley, Calif., assigned to the project by the U. S. Public Health Service, will be principal collectors of specimens.

WEST VIRGINIA

Campaign Against Air Pollution.—A panel truck designed by the Bureau of Industrial Hygiene is to be used in the study of atmospheric contamination in West Virginia cities. The new unit makes it possible to collect air-borne samples of materials previously unobtainable by use of settling cans. During the experimental stage the unit will be located in Kanawha County. Later it will be used for the investigation of atmospheric complaints which are frequently reported by county and district health units.

WISCONSIN

University Appointment.—John W. Barnard, Ph.D., has been appointed associate professor of physiology in the University of Wisconsin Medical School, Madison. Dr. Barnard obtained his Ph.D. in neuroanatomy from the University of Michigan, Ann Arbor, 1935. He has taught at various medical schools.

Personals.—Dr. Raymond J. Rogers, Oconto, has been awarded a four month fellowship in exfoliative cytology at the Mayo Clinic, Rochester, Minn., under the sponsorship of the American Cancer Society.——Dr. Cornelius A. Harper, Madison, former state health officer, has been cited for his pioneer work in public health by the National Society for the Prevention of Blindness, in which he was given an honorary membership.——Dr. Herbert C. Johnston, assistant medical director of St. Ann's Hospital at St. Ann de Bellevue, Quebec, Canada, has been appointed assistant superintendent of Wisconsin General Hospital, Madison. A 1937 graduate of McGill University, Dr. Johnston entered Canadian military service in 1939 and served in England, Sicily and Italy. Since that time he has been associated with the Canadian department of veteran affairs. He will assume his duties immediately.

PUERTO RICO

Puerto Rico Medical Association Proceedings.—At the annual meeting of this association in San Juan, December 14-18, the chamber of delegates reiterated the endorsement of the medical profession of Puerto Rico to the new school of medicine to be established at the University of Puerto Rico.

The delegates also authorized a committee composed of Drs. Rafael A. Vilar, William R. Gelpi, Héctor A. Bladuell, Carlos A. Quilichini, A. Lacot Salgado and M. Fernández Fuster to study a plan for the organization of medical services for the benefit of the community, either through the Blue Cross Plan of Puerto Rico or as a separate entity. The operation of such a plan will be under the immediate direction and supervision of the board of directors of the Puerto Rico Medical Association to give opportunity to all its members to participate in such organization. The chamber of delegates also approved associate membership to facilitate participation by interns and resident physicians in the activities of the association.

Dr. Ignacio Chavez, México, D. F., was named honorary member of the Puerto Rico Medical Association. He came to Puerto Rico to give lectures on cardiology for a period of two weeks and for the benefit of the local medical profession. The following officers were elected: Drs. A. Oliveras Guerra, president; Francisco Berio, vice president; Victor Montilla, secretary; Guillermo Barbosa, treasurer; Manuel Astor, speaker of the chamber of delegates, and Dr. Manuel Guzmán Rodríguez, delegates to the American Medical Association.

ALASKA

Organize Water Pollution Board.—A six member Alaska Water Pollution Board was formed by the last territorial legislature to administer the Water Pollution Act. Dr. C. Earl Albrecht, commissioner of health, was appointed executive secretary. The board's next function is to determine standards of water purity. Plans for the construction, extension, installation or operation of any territorial sewage system or treatment works now require approval by the board.

GENERAL

Monthly Publication for Surgeons' Journal.—Beginning with the January issue, *The Journal of the International College of Surgeons* will appear as a monthly. Heretofore it has been published every two months or as a quarterly.

Sioux Valley Medical Association.—The annual meeting of this association of physicians in the Sioux Valley area of South Dakota, Minnesota, Nebraska and Iowa will be held in Sioux City, Iowa, at the Hotel Martin, January 24-26.

Dr. Lotka Dies.—Alfred J. Lotka, D.Sc., who from 1924 until his death was associated with the statistical bureau of the Metropolitan Life Insurance Company, died December 5 in Red Bank, N. J. With Louis I. Dublin, Ph.D., he wrote extensively on population trends.

Meeting on Surgery of the Hand.—The American Society for Surgery of the Hand will hold its annual meeting February 10 at the New York Academy of Medicine building, New York. Those presenting papers by invitation include:

Erik Moberg, Göteborg, Sweden, Brachial Block Anesthesia with Xylocain.
William K. Gregory, Ph.D., New York, Phylogeny of the Hand.
Emanuel B. Kaplan, New York, Early Development of the Hand and Its Relation to Function.
Vernon Luck, Los Angeles, Subcutaneous Faciotomy in Dupuytren's Contracture (Motion Picture).

American Board of Psychiatry and Neurology.—During 1950 this board will conduct two examinations. The first examination will be June 23-24 in San Francisco, preceding the convention of the American Medical Association. Applications for this examination must be in the secretary's office before March 15. The second will be held in the East in December. No applications for this examination will be accepted after September 1. The first 300 eligible applicants will be accepted, and those remaining will be deferred until 1951.

Many specialists certified by the American Board of Psychiatry and Neurology, Inc., have changed locations since certification. It is essential that the secretary have correct

addresses and diploma numbers for the purpose of directing correspondence. This information should be sent at once to J. J. Braceland, M.D., Secretary, 102-110 Second Ave., S.W., Rochester, Minn.

Gastroenterologic Association Contest. — The National Gastroenterological Association announces its annual cash prize award contest for 1950. One hundred dollars and a certificate of merit will be given for the best unpublished contribution on gastroenterology or allied subjects. Contestants residing in the United States must be members of the American Medical Association and those residing in foreign countries must be members of a similar organization in their own country. The award is to be made at the annual convention banquet of the association in October. The association reserves the right of publishing the winning contribution and those receiving certificates of merit in its official publication, *The Review of Gastroenterology*. Entries for the 1950 prize should be limited to 5,000 words, be typewritten in English and submitted in five copies accompanied with an entry letter and must be received by the National Gastroenterological Association, 1819 Broadway, New York 23, not later than June 1.

Fellowships in Atomic Medical Science.—The National Research Council has announced a modified program of postdoctoral research fellowships in the medical sciences supported by the Atomic Energy Commission. A fellow must be a citizen of the United States under 35 years of age at the time of appointment. He or she must have had training in some branch of the biologic or medical sciences equivalent to that represented by the M.D. or Ph.D. degree and must present promise of research ability. Holders of the M.D. degree must have completed one year of internship or work which, in the opinion of the board, is equivalent (see THE JOURNAL, January 7, page 39).

Appointments will be for one year unless a shorter term is approved by the Fellowship Board and must terminate on or before June 30, 1951. Requests for application blanks should be addressed to the AEC Postdoctoral Fellowship Board in the Medical Sciences, National Research Council, 2101 Constitution Avenue, Washington 25, D. C. Applications must be completed by February 15.

Expert Committee on Plague.—Dr. Georges Blanc, director of the Pasteur Institute of Morocco, has prepared an article for the World Health Organization in which he states that an expert committee on plague has been formed by WHO for the purpose of combining all known methods of attack against plague. During a recent meeting of this committee, held at WHO headquarters in Geneva, a system was planned for the compilation and assessment of all existing data, the carrying out of full treatment measures and the detailing of methods of eradication of plague centers.

It is planned that a group of specialists in this field will be sent to India, where the disease today presents a grave problem. There they will demonstrate plague eradication work for the first time on an international scale. Demonstration areas for plague eradication recommended by the WHO Expert Committee include one of the infected islands off the coast of Africa (Azores or Madagascar) Morocco, the Belgian Congo and China. In these plague centers the use of DDT, "1080" (sodium fluoracetate) and streptomycin, combined with the knowledge available today, will demonstrate the ability of modern science to conquer one of man's most dreaded enemies.

Conference on Medical Service. — The National Conference on Medical Service will meet February 5 at the Palmer House, Chicago, under the presidency of Dr. John S. Bouslog, Denver. The program is as follows:

Congressman James I. Dolliver, Fort Dodge, Iowa, Personal Observations of Socialized Medicine in England.
Warren F. Draper, Arlington, Va., Medical Program of the United Mine Workers of America Welfare and Retirement Fund.
Mr. Allan Kline, Chicago, president, American Farm Bureau Federation, Medical Problems of the American Farmer.
Mr. George E. Brand, Detroit, member board of governors, American Bar Association, Preservation of the Professions.
Mr. Ray D. Murphy, New York, vice president and actuary, Equitable Life Assurance Society of the United States, Problems Arising in Meeting the Challenge of Compulsory Health Insurance.
Philip Adams, D.D.S., Boston, president, American Dental Association, A Positive Program to Improve Dental Health.
Mr. William H. Book, Indianapolis, president, American Chamber of Commerce Executives, The Doctor and His Community.
Joseph Lawrence, Washington, D. C., Office, American Medical Association, Developments in Washington.

Dr. George F. Lull, Secretary and General Manager, and Dr. Ernest E. Irons, President, American Medical Association, Chicago, will represent the association on the program.

Speakers at the conference are largely leaders of groups outside the medical profession; the conference was so planned in order that their viewpoints in regard to problems concerning medical service may be heard.

Red Cross Blood Program.—At the end of its second year of operation, the National Blood Program of the American Red Cross is supplying blood to 1,550 hospitals in 35 states. More than 500,000 pints of blood have been provided through the 30 regional programs in operation. Blood supplied through Red Cross centers is taken from voluntary donors, tested as to medical safety, typed as to blood group and Rh factor and provided to physicians and hospitals without charge. Care has been taken to assure use of all blood collected, either for transfusion or as a source for blood plasma. In addition to whole blood, large quantities of blood components have been distributed. During the last fiscal year 688,532 units of immune serum globulin were distributed by the Red Cross through state health departments. Enough of the globulin was provided for treatment in every reported case of measles during the so-called measles season. The country generally is reaping benefits from these derivatives processed from the surplus plasma returned by the armed forces at the end of the war. The surplus plasma from which derivatives are produced is now running low. By the end of another year it will be necessary for regional blood centers to meet the day by day needs for whole blood and try to meet the increased demands for blood derivatives. On January 1 regional blood centers were operating at Rochester, N. Y.; Wichita, Kan.; Stockton, Calif.; Atlanta, Ga.; Washington, D. C.; Los Angeles; Tucson, Ariz.; San Jose, Calif.; Omaha; Springfield, Mo.; St. Louis; Charlotte, N. C.; Lansing, Mich.; Detroit; Yakima, Wash.; Great Falls, Mont.; Columbus, Ohio; St. Paul; Nashville, Tenn.; Portland, Ore.; Boise, Idaho; Philadelphia; Asheville, N. C.; Louisville, Ky.; Syracuse, N. Y.; Mobile, Ala.; Johnstown, Penn.; Savannah, Ga., and Norfolk, Va. The program is also operating on a statewide basis in Massachusetts.

LATIN AMERICA

National Lottery Provides Health Mobile Units.—The government of Cuba has received the first shipment of its 108 specially designed motor coaches that will give medical and dental services to 100,000 children in poor rural areas. Each mobile unit consists of three vehicles, a medical and dental coach, an ambulance and living quarters for the medical team of six persons. The government will send the units into areas where hospital, medical and dental facilities are lacking. Particular attention will be given to tests for tuberculosis and blood and skin diseases. Mobile unit teams will also treat communicable diseases, give dental services and engage in preventive medicine. Patients with chronic diseases or those in need of serious operations will be taken to the nearest hospital in the unit's ambulance. The units are staffed with a surgeon, physician, dentist, technician and two nurses. The project is expected to cost the government $3,000,000, receipts of the Cuban National Lottery.

CORRECTION

Position of the Foot.—Under this title in Queries and Minor Notes in THE JOURNAL Dec. 17, 1949, page 1197, in the sentence "When a foot is everted and adducted . . ." the word "everted" should have read "inverted."

Dr. Haserick.—In the Current Comment entitled "Diagnosis of Acute Disseminated Lupus Erythematosus" in THE JOURNAL, Dec. 17, 1949, page 1158, an author's name was misspelled in both footnotes and in the body of the Current Comment. The proper spelling is J. R. Haserick, and not as it appeared, Hasenik.

Marriages

EUGENE JOSEPH FITZPATRICK JR., New Haven, Conn., to Miss Margaret Elizabeth Moore of Greenwich, November 12.

WILLIAM FRANCIS HUGHES, Pitman, N. J., to Miss Beatrice Christine Zilly of Southington, Conn., November 12.

LEWIS KITCHENER DAHL, New York, to Miss Marilyn Louise Cupp of South Orange, N. J., November 12.

JOHN HANEY KELLER, China Grove, N. C., to Miss Margaret Liluer Beale of Franklin, December 3.

EDWARD COLTON MEEK JR., Seattle, to Miss Elizabeth Jean Ward of Portland, Ore., November 19.

GEORGE JEFFERSON AUSTIN JR., Moultrie, Ga., to Miss Evelyn Saunders of Valdosta, November 19.

RICHARD EDWARDS GORDON, New York, to Miss Katherine Lowman Kline of Cuba, November 12.

Deaths

Archibald Barklie Coulter ✦ Washington, D. C.; born in Baltimore in 1897; Johns Hopkins University School of Medicine, Baltimore, 1924; member of the American College of Chest Physicians, American Trudeau Society and the American Public Health Association; served on the board of directors of the District Tuberculosis Association; formerly on the faculty of Georgetown University School of Medicine and Howard University College of Medicine; served as director of the bureau of tuberculosis of the health department of the district and as tuberculosis coordinator of the district; at one time a member of the Trudeau Sanatorium staff in Saranac Lake, N. Y., and associated with Gallinger Municipal Hospital in Washington, D. C.; died December 7, aged 52, of coronary sclerosis.

John William Duncan ✦ Elkhorn, Neb.; born Roseland, Neb., Dec. 23, 1889; John A. Creighton Medical College, Omaha, 1912; past president of the Omaha-Douglas Counties Medical Society; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; member of the Western Surgical Association; for many years practiced in Omaha, where he was on the faculty of his alma mater, now known as the Creighton University School of Medicine, and on the staffs of Douglas County Hospital, St. Catherine's Hospital, Children's Memorial Hospital and St. Joseph's Hospital, where he died November 20, aged 59, of cerebral hemorrhage, hypertension and arteriosclerosis.

Atchison Almond Ashby, Sioux City, Iowa; Rush Medical College, Chicago, 1883; member of the American Medical Association; died in St. Joseph's Hospital November 9, aged 88, of cerebral thrombosis.

Man Hing Au, Honolulu, Hawaii; Washington University School of Medicine, St. Louis, 1949; served during World War II; intern at Cincinnati General Hospital, where he died November 23, aged 35, of cancer.

Eusebius Marion Barron, Nashville, Tenn.; Meharry Medical College, Nashville, 1948; interned at George W. Hubbard Hospital of Meharry Medical College, where he died November 28, aged 38, of neuroblastoma with metastases.

William David Baun ✦ Philadelphia; Jefferson Medical College of Philadelphia, 1915; also a graduate in pharmacy; served during World War I; physician for the draft board during World War II; affiliated with Frankford Hospital; died October 19, aged 60, of cerebral thrombosis.

Oscar Joseph Bienvenu, Opelousas, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1924; member of the American Medical Association; president and formerly secretary of St. Landry Parish Medical Society; served during World Wars I and II; owner of St. Rita's Infirmary; died in Baptist Hospital, New Orleans, November 6, aged 50, of congestive heart failure.

Clarence Lavan Bittner ✦ Sacramento, Calif.; Jefferson Medical College of Philadelphia, 1914; served during World War I; died November 26, aged 62, of coronary occlusion.

Toria J. Bratten, Woodbury, Tenn.; University of Tennessee Medical Department, Nashville, 1905; for many years county health officer; died in Good Samaritan Hospital November 15, aged 69, of coronary heart disease with infarction.

Herbert Leigh Buckles, Hartford City, Ind.; Starling-Ohio Medical College, Columbus, 1914; chief of staff of Blackford County Hospital; member of the board of directors of the Indiana State Tuberculosis Association; formerly member of the school board; served during World War I; died in St. John's Hickey Memorial Hospital, Anderson, November 24, aged 65, of adenocarcinoma of the colon.

Virgil Lewis Chambers ✦ Huntington, W. Va.; University of Louisville (Ky.) School of Medicine, 1926; member of the American Association of Industrial Physicians and Surgeons; medical director and vice president of the Appalachian Life Insurance Company; affiliated with St. Mary's and Huntington Memorial hospitals; died suddenly November 30, aged 54, of coronary occlusion.

Frank Lee Clymer, Cumberland, Md.; University of Maryland School of Medicine, Baltimore, 1886; died recently, aged 84.

Thomas Lyttleton Cockrell ✦ Hinsdale, Mont.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1908; affiliated with Frances Mahon Deaconess Hospital, Glasgow; died in Deaconess Hospital, Great Falls, November 18, aged 64, of myocardial infarction.

George Aloysius Connor, Cambridge, Mass.; (licensed in Massachusetts in 1911); died recently aged 63, of coronary thrombosis.

Henry Apple Conway, Beverly Hills, Calif.; College of Physicians and Surgeons of San Francisco, 1918; served during World War I; for many years affiliated with Cedars of Lebanon Hospital in Los Angeles; died November 14, aged 56, of acute leukemia.

James Edward Crawford, Tulia, Texas; Southwestern University Medical College, Dallas, 1906; died October 21, aged 78, of cardiac decompensation.

Edwin R. Cutler, Basalt, Idaho; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; member of the American Medical Association; died November 16, aged 81, of coronary occlusion.

Wade Corperal Dansey, Sedalia, Mo.; University of West Tennessee College of Medicine and Surgery, Memphis, 1915; died November 21, aged 63, of coronary thrombosis.

Joseph Davidson ✦ New York; College of Physicians and Surgeons, medical department of Columbia College, New York, 1892; for many years on the staff of Mount Sinai Hospital; died November 30, aged 79, of disease of the liver.

Thayer Clinton Davis, Wadena, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1913; member of the American Medical Association; on the staff of Wesley Hospital; president of the First National Bank; died November 18, aged 62, of heart disease.

Jesse L. Eaton, St. Louis; Missouri Medical College, St. Louis, 1884; formerly superintendent of State Hospital number 4 in Farmington; died recently, aged 85.

Alexander C. Flack ✦ Fredonia, Kan.; Medical College of Ohio, Cincinnati, 1885; served as a member and president of the school board; past president of the Wilson County Medical Society; died November 14, aged 91, of cardiovascular renal disease and arteriosclerosis.

James Carlisle Fleming ✦ Pittsburgh; University of Pittsburgh School of Medicine, 1910; affiliated with Passavant Hospital; died in St. Anthony's Hospital, St. Petersburg, Fla., November 13, aged 65, of cardiovascular disease.

John Alva Fuson ✦ Mansfield, Mo.; Barnes Medical College, St. Louis, 1905; died November 15, aged 74, of myocardial infarction.

Ulysses Grant Gifford ✦ Kennett Square, Pa.; Jefferson Medical College of Philadelphia, 1888; member of the American Heart Association; affiliated with Chester County Hospital, West Chester, where he died November 22, aged 87.

Morton Kay Green, Waunakee, Wis.; Rush Medical College, Chicago, 1901; member of the American Medical Association; for many years medical superintendent of the Mendota (Wis.) State Hospital; died November 21, aged 72.

James Kuykendall Guthrie ✦ Martinsburg, W. Va.; College of Physicians and Surgeons, Baltimore, 1912; died December 5, aged 62, of heart disease.

Lily Kinnier Haisch ✦ Dubuque, Iowa; Northwestern University Woman's Medical School, Chicago, 1899; past president of the Dubuque County Medical Society; found dead November 26, aged 73.

George Kennedy Hays, Monongahela, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1903; served with the British Expeditionary Forces during World War I; on the staff of Memorial Hospital; for many years vice president of the Bentleyville National Bank; died November 20, aged 67.

Thomas Wilburn Holmes, Winona, Miss.; Vanderbilt University School of Medicine, Nashville, 1915; fellow of the American College of Surgeons; served overseas during World War I; for many years affiliated with Winona Infirmary, where he died November 25, aged 58, of cerebral hemorrhage.

Elias Holovtchiner, Omaha; Universität Leipzig Medizinische Fakultät, Saxony, Germany, 1886; died in Plattsmouth December 2, aged 89.

Albert E. Hubbard, Buffalo; University of Buffalo School of Medicine, 1894; formerly associated with the U. S. Public Health Service; for many years on the staff of the U. S. Marine Hospital; died November 26, aged 80, of coronary thrombosis.

William Henderson Jasper, Senior Assistant Surgeon, U. S. Public Health Service, reserve, Takao, Formosa; Northwestern University Medical School, Chicago, 1947; interned at St. Luke's Hospital in Chicago; died October 19, aged 28, of pneumonia.

✦ Indicates Fellow of the American Medical Association.

Harry F. Kaack ⊕ Clinton, Iowa; the Hahnemann Medical College and Hospital, Chicago, 1910; died November 1, aged 68.

Arthur Gaetano Keane, New York; University and Bellevue Hospital Medical College, New York, 1900; member of the American Medical Association; for many years instructor in clinical surgery at his alma mater; died November 25, aged 73, of heart failure.

Harry Edward Kilgus, Brockway, Pa.; Jefferson Medical College of Philadelphia, 1904; member of the Pennsylvania Game Commission and school board; died in the Williamsport (Pa.) Hospital November 12, aged 70, of sarcoma of the ileum and prostatic hypertrophy.

John DeWitt King, Durham, N. C.; Washington University School of Medicine, St. Louis, 1947; interned at Syracuse (N. Y.) University Medical Center; intern at Duke Hospital; killed November 19, aged 24, when an automobile in which he was driving overturned.

Rinhart F. Kippenberger ⊕ Scott City, Kan.; University of Oklahoma School of Medicine, Oklahoma City, 1927; died November 21, aged 51, of cerebral hemorrhage.

Joseph Krobalski, Lynn, Mass.; College of Physicians and Surgeons, Boston, 1924; member of the American Medical Association; died recently, aged 56, of coronary occlusion.

Paul Herman Lippold, Detroit; Detroit College of Medicine and Surgery, 1916; member of the American Medical Association; fellow of the American College of Surgeons; served during World War I; affiliated with Grace Hospital; died November 15, aged 59, of heart disease.

Angelo Lo Schiavo, Brooklyn; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1920; member of the American Medical Association; died November 20, aged 54, of coronary thrombosis.

William Lowe, Madison, S. D.; Chicago Homeopathic Medical College, 1889; formerly postmaster; died November 14, aged 88.

Eugene Ambrose McCarthy ⊕ Fall River, Mass.; Harvard Medical School, Boston, 1908; member of the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; formerly assistant city physician; visiting orthopedic surgeon, Newport (R. I.) Hospital; on the staff of the Union Hospital; associated with Rocky Farm Camp for Crippled Children in Newport, R. I.; died November 30, aged 68.

William Edward Roche McMahon, Boston; Harvard Medical School, Boston, 1916; member of the American Medical Association; served during World War I; police physician; died November 19, aged 61.

Charles Francis Mahood, Alderson, W. Va.; University College of Medicine, Richmond, 1901; member of the American Medical Association; formerly secretary of the Greenbrier Valley Medical Society; served during World War I; health officer and member of the city council; died December 14, aged 71.

Franz Andrew Maroshek ⊕ Las Vegas, Nev.; Temple University School of Medicine, Philadelphia, 1945; served as city health officer; died in the Temple University Hospital, Philadelphia, November 16, aged 35.

Louis E. Meyer ⊕ Thibodaux, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1889; died in St. Joseph's Hospital December 1, aged 86, of carcinoma of the prostate.

Charles A. Mohr ⊕ Mobile, Ala.; Medical College of Alabama, Mobile, 1884; past president of the Mobile County Medical Society; for many years county health officer; member of the board of trustees of the Alabama state hospitals; at one time on the faculty of his alma mater; found dead November 28, aged 92, of myocarditis.

Edward Louis Myers, Woonsocket, R. I.; born in Woonsocket, R. I., Dec. 9, 1885; Tufts College Medical School, Boston, 1910; member of the American Medical Association; formerly member and chairman of the school committee; for many years medical examiner; an officer in the U. S. Army during World War I; served as police surgeon, a school medical inspector and examining physician for the police and fire departments; affiliated with Woonsocket Hospital; died November 10, aged 63, of myocarditis and hypertension.

Percy Carl Neumlist, Old Monroe, Mo.; St. Louis College of Physicians and Surgeons, 1914; member of the American Medical Association; served during World War I; killed November 21, aged 61, in an automobile accident.

Arthur Joseph Neunann ⊕ Detroit; Chicago College of Medicine and Surgery, 1917; died in St. Mary's Hospital November 28, aged 58.

Frederick William Noble, Fort Madison, Iowa; Saginaw (Mich.) Valley Medical College, 1899; Northwestern University Medical School, Chicago, 1906; died November 5, aged 73.

Julius Abraham Oshlag ⊕ Miami Beach, Fla.; University and Bellevue Hospital Medical College, New York, 1930; specialist certified by the American Board of Internal Medicine; served in the medical corps of the U. S. Naval Reserve 1942-1943 and later in the U. S. Public Health Service reserve during World War II; affiliated with Mount Sinai and St. Francis hospitals; died suddenly, November 9, aged 43, of coronary occlusion.

Whyte Glendower Owen, White Castle, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1880; member of the American Medical Association and in 1903 a member of its House of Delegates; at various times president of the state board of health; served during World War I; a representative to the International Congress of Tuberculosis in London and delegate to the International Sanitary Conference in Mexico, D. F.; died November 20, aged 91.

Ludwig Louis Parker, Albany, N. Y.; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Germany, 1910; member of the American Medical Association; affiliated with Memorial Hospital; died November 17, aged 65, of coronary thrombosis.

Robert H. Peters, Mobile, Ala.; Medical College of Alabama, Mobile, 1894; served as secretary of the Mobile County Medical Society; died in a hospital November 9, aged 78, of adenoma of the pituitary.

Joseph Francis Poheim, San Francisco; Cooper Medical College, San Francisco, 1898; served as chief of the city physicians of San Francisco; member of the American Medical Association; died in St. Joseph's Hospital November 14, aged 72.

John R. Pusey, Toronto, Kan.; Louisville (Ky.) Medical College, 1901; served as county health officer; died November 16, aged 70, of coronary thrombosis.

Jose Maria Ramirez, Cheyenne, Wyo.; Jenner Medical College, Chicago, 1916; died in the Memorial Hospital of Laramie County November 16, aged 72, of cardiac decompensation.

John Silas Rankin, Portland, Ore.; Eclectic Medical Institute, Cincinnati, 1902; member of the American Medical Association; served during World Wars I and II; division surgeon for the Southern Pacific Railroad; on the staff of the Good Samaritan Hospital; died November 7, aged 71.

William Harris Rendleman ⊕ Davenport, Iowa; Rush Medical College, Chicago, 1904; past president and secretary of the Scott County Medical Society and of the Iowa-Illinois Central District Medical Society; past president of the Iowa Clinical Medical Society; member of the staffs of St. Luke's Hospital and the Mercy Hospital, where he died November 14, aged 69, of coronary sclerosis.

Ralph Frederic Reno, Cincinnati; Cincinnati College of Medicine and Surgery, 1897; died in the Bethesda Hospital October 12, aged 76, of bronchopneumonia and petit mal epilepsy.

Otto Ernest Frederick Risch ⊕ Brooklyn; Long Island College Hospital, Brooklyn, 1887; an Associate Fellow of the American Medical Association; affiliated with Caledonian Hospital; died November 30, aged 85, of carcinoma of the pancreas.

Ernest Victor Rittenhouse, Orford, N. H.; Illinois Medical College, Chicago, 1900; died in State Hospital, Concord, recently, aged 73, of cerebral arteriosclerosis.

John Lorenzo D. Roberts, Seaside, Calif.; University of the City of New York Medical Department, New York, 1885; for many years on the school board; died November 21, aged 86.

Henry Clark Sanders, Selmer, Tenn.; Vanderbilt University School of Medicine, Nashville, 1894; member of the American Medical Association; a trustee for Union University, Jackson; died November 16, aged 81, of myocarditis.

William Bement Stem, Boston; Yale University School of Medicine, New Haven, 1945; served during World War II; resident physician at the Children's Hospital; died November 28, aged 31.

Andrew J. P. Wilson, Wheeling, W. Va.; University of Pennsylvania Department of Medicine, Philadelphia, 1894; died November 17, aged 81, of coronary occlusion.

Frank Alter Zibelman, Chicago; Chicago College of Medicine and Surgery, 1917; member of the American Medical Association; died November 19, aged 56, of coronary thrombosis.

Foreign Letters

PARIS

(From Our Regular Correspondent)

Nov. 7, 1949.

A New Bill for Fighting Abortion

A new bill intensifying the fight against abortion has been drafted and will be soon discussed in the House. The first articles of the scheme have given rise to ardent discussions among the members of the medical profession.

Article 1.—"All doctors or midwives are under obligation to declare within forty-eight hours all cases of interruption of pregnancy, even not provoked, seen or treated in the exercise of their profession, outside hospitals. Neither the name of the person nor the place where abortion occurred are to appear in the declaration. Declarations are to be forwarded to the Council of the Order of Doctors through the district director of public health.

Article 2.—The 1939 law is amended as follows: As regards offenses under article 317 of the penal code the right of direct summoning and the right to appear as party to the case is awarded to organizations of doctors, pharmacists or midwives.

Article 3.—Doctors, midwives, dental surgeons and pharmacists are bound to declare immediately the activities of persons practicing abortion. The declaration is to be made to the president of the order of the profession to which the declarer belongs. The president must forward the declaration immediately to the judicial authority, with his remarks, if necessary, without mention of the name of the person who had the abortion or the name of the declarer except on authorization of the latter. The president will have to remit to the declarer the receipt of the public prosecutor.

Some doctors have protested these dispositions as dangerous. They consider that such a compulsory declaration, even without mention of the name of the person concerned or the place, is a threat against professional secrecy. Since an examining magistrate is entitled to search the files of the order, he will thus be enabled to find out the name of the doctor, the place where he practices and in some cases the name of the woman. When it becomes common knowledge that the doctor is reporting all cases of miscarriage, women, even in the event of spontaneous miscarriage, will hesitate to call the doctor; this may result in infections causing sterility and possibly death. The doctors opposing the scheme also say that they repudiate the idea of denouncing a fellow doctor by applying article 3 and also sending anonymous letters to the public prosecutor reporting persons outside the medical profession who practice abortion. The opposition stresses also that the doctor who reports the abortion is only the witness of the consequences of the abortive procedures and that, as his declaration will be based on hearsay, it will have only doubtful value. It also states that the denunciation ought not to be required from a doctor, whom a patient consults whatever the cause of her disease.

Lysis of Cicatricial Tissues

Vagliano and G. Tsiro have observed, over several years, the remarkable and lasting action of sodium citrate in 3,000 cases of arteritis obliterans. They also noted that the same substance effects the disappearance of cicatricial tissue, sequela of lesions due to severe frostbite. They tried sodium citrate on dogs on which they artificially provoked scars. The animals received every other day for two months 10 cc. of a 1 or 2 per cent solution of sodium citrate intravenously. They noted the complete disappearance of the scars and their replacement by "normal" tissue which had neither hair nor glands. They found that in collagenous or connective fibers with rare nuclei of the cicatrix there occurred multiplication of the nuclei of these cells, which take a triangular form and, after one month of treatment, rarefaction of all the cicatricial tissue. These experiments, reported by the authors at the Oct. 17, 1949 meeting of the Academy of Sciences, may offer a new method for the treatment of exaggerated cicatrices and of keloids.

Suprarenal Origin of the Masculinizing Syndrome

S. Blondin reported on May 18, 1949, before the Academy of Surgery the cases of 3 women, 38, 28 and 16 years of age, presenting a typical masculinizing syndrome. After careful examinations had revealed no hypophyseal or ovarian origin, the author investigated a suprarenal origin and, after urography and aortography, he performed an epinephrectomy. In 2 patients he found hypertrophy of the gland and histologically proved hyperplasia of the spongiocytal layer; in the third patient he found a suprarenal tumor with the histologic appearance of an adenoma. The suprarenalectomy was well tolerated by the patients, whose condition became improved. The choice of the side on which the operation is to be performed is indicated by urography, radiography after pneumopyelography and aortography. Blondin has emphasized the importance of this observation, which has cast further light on the pathogenesis of Cushing's disease.

Diagnosis of Mediastinal Tumors

The differential diagnosis between mediastinal tumors and aneurysms often is difficult. M. Marchal proposes a photoelectric method. The principle of this new method is based on the fact that pulsations peculiar to aneurysms retain always the same general form and the same timing, uninfluenced by the inspiratory time or the position, vertical or horizontal, of the patient. Tumors coupled with the cardiovascular shadow, on the other hand, have pulsations, the form and the timing of which vary according to the displacement of the heart. Detection is by means of the simultaneous registering of the electrocardiogram. Even tumors appearing as not pulsatile at radioscopy may produce, through the intermediary of the photoelectric cell, a characteristic pulsation. At the March 6, 1949 meeting of the Society of Cardiology, the author reported a series of cases in which the diagnosis had been made with this method; several of the diagnoses had been confirmed at operation.

TURKEY

(From Our Regular Correspondent)

ANKARA, Dec. 5, 1949.

Barbiturates in General Anesthesia

Dr. Tarik Maktav, chief obstetrician of the Eskişehir Maternity Hospital, obtained good results with kemithal sodium (sodium cyclohexenyl-allyl-thiobarbiturate), narconumal (sodium salt of 1 methyl-5,5-allyl-isopropylbarbituric acid), hexobarbital sodium and thiopental sodium in 25 operations involving 4 cysts, 4 prolapses of the uterus, 3 ectopic pregnancies, 3 fixed retroversions, 3 minor operations, 2 myomas, 2 hernias, 1 basiotripsy, 1 appendectomy, 1 exploratory laparotomy and 1 phlegmon. In 9 cases kemithal sodium, in 8 cases narconumal, in 5 cases hexobarbital sodium and in 3 cases pentothal sodium was used. For the intravenous injections only a fresh preparation with twice distilled water was used; solutions with slight sedimentation were rejected. The barbiturates did not cause any untoward effects on the patients, who slept well the night after the operation without sedatives. On the average the patients were conscious in two to three hours; they were free from nausea, vomiting or coughing, and respiratory depressions were minimal. One patient had a slight laryngeal spasm, which passed after the patient's head was lowered. When the injection is given, the blood pressure falls but immediately becomes normal again. The electro-

cardiograms at the time of the injection, during the operation and at the end of operation did not reveal any change, although the pulse rate rose for a brief period. The dosage administered depended on whether the operation was of short or long duration and on the patient's condition. On the night before the operation the patient was given an enema but no sedative. An hour before the operation morphine and atropine were given and shortly before the operation the patients were asked to urinate. Thiopental sodium was used in 2.5 to 5 per cent solution, kemithal sodium in a 5 to 10 per cent solution and narconumal and hexobarbital sodium in a 10 per cent solution. On the average the patients received 3 Gm. In 1 case, an ectopic pregnancy, the patient was inadvertently given 5 Gm.; she became cyanotic and respiration stopped, but the heart continued to function apparently normally. Artificial respiration was applied and the operation successfully completed.

Modern methods of anesthesia are not yet in general use in Turkey. Local, regional or spinal anesthesia usually is employed and sometimes chloroform or a mixture of chloroform and ether. Anesthetics are given by interns or experienced nurses or midwives. Untoward effects due to the older methods of anesthesia are extremely rare.

The Ministry of Health and Social Assistance has recently purchased from Sweden a modern apparatus for the ministry's Istanbul Haidar Pasha model hospital, where special courses will be held by the Swedish anethesiologist. The lack of funds for modern apparatus has hitherto prevented the adoption of modern methods of anesthesia and the training of anesthesiologists.

THE NETHERLANDS

(From Our Regular Correspondent)

Nov. 24, 1949.

Smallpox Reinfection in Indonesia

Before the war many epidemic diseases, e. g., malaria, plague, smallpox, yaws and ancylostomiasis, were kept on a low level in the Netherlands East Indies. A striking example of this success was evident in the campaign against smallpox. This disease was completely stamped out many years ago by an organization which was founded about a century ago. The basic principle of this organization consisted of creating many hundreds of vaccination districts. Within each of these districts a well trained native vaccinater visited his vaccination centers four times a year, vaccinating especially babies 6 to 9 months old. In the year 1939, for instance, the number of vaccinations mounted to more than 2,000,000 and the number of revaccinations to 5,600,000. During the Japanese occupation this organization broke down and after the war it was never reconstructed.

The spread of smallpox from Malacca to Sumatra (1947) and to Java a year later revealed that revaccination had been neglected in Indonesia. In January 1949 the disease was recognized in Batavia, and in the first half of the year there were thousands of cases. There is no immediate hope of stamping it out again.

A Rare Case of Besnier-Boeck Disease

In the Clinical Society, Rotterdam, Van Rijssel (Groningen) described the case of a 53 year old woman suspected of having ventricular cancer. After resection, examination of the stomach revealed stenosis of the pylorus and thickening of the prepyloric region, caused by a large number of tuberculoid foci, especially in the mucosa and submucosa, with a few in the muscular part of the wall of the stomach and subserously. In the centers of these foci giant Langerhans cells and Schaumann's corpuscles were present; necrosis and caseation were not seen. Slightly enlarged nodes on the minor curvature contained epithelioid cells; tubercle bacilli were not found. Some facts in the patient's history supported the diagnosis of Besnier-Boeck's disease. For many years she had been under the observation of a tuberculosis clinic, where radiographic examination showed many fibrous spots in the lungs and a negative reaction to tuberculin had been elicited. Four years previously a laparotomy had revealed pancreatitis. Stenosis of the pylorus as a complication of Besnier-Boeck's disease seems to be rare. The author could not find an analogous case in the medical literature.

Treatment of Toxoplasmosis

P. H. Van Thiel (Leyden) studied the therapeutic effect of several sulfonamide compounds, arsenic compounds and antimalaria drugs on mice intracerebrally or intraperitoneally infected with a Toxoplasma hominis strain isolated by the author. He confirmed what Sabin and Warren had found: that only sulfonamide drugs give good results, particularly the three pyrimidines, sulfamerazine, sulfamethazine and sulfadiazine. In human beings, Van Thiel recommends parenteral injection with sulfamerazine. In mice, recovery after treatment is not always complete. In many cases the resistance of the animal after treatment is due to latent infection.

A Streetcar Mystery

Last summer the dermatologists in Amsterdam were often consulted by female patients showing a pathologic condition of the skin of the calves. Professor Prakken, invited by the municipality to solve this problem, found that these patients regularly used the same streetcar line at the same hour. Inside the wooden construction of the seats of the cars nests of bugs were discovered.

Professor Brouwer Dies

Prof. B. Brouwer, outstanding neurologist in the University of Amsterdam and director of the Central Institute for Brain Research, died November 1, at the age of 68. He was internationally known. This past year he had lectured in Switzerland, had been a guest of the Royal Society of Medicine (London) and had attended the congress in Paris. He had many friends in the United States.

SWITZERLAND

(From Our Regular Correspondent)

GENEVA, Nov. 21, 1949.

Nobel Prize for Medicine Awarded to a Swiss Physician

Prof. Walther Rudolf Hess, who recently received with Professor Moniz (Lisbon,Portugal) the Nobel Prize for Medicine, was born in Frauenfeld on March 17, 1881. He practiced ophthalmology in Germany and in Switzerland and in 1917 was named director of the Physiologic Institute of the Zurich University.

As a great searcher and lively teacher, Professor Hess has taught a large number of physiologists who now are working in Switzerland and abroad; he is well known for his work on the respiratory tract, blood circulation, physiologic optics and, above all, experimental physiology of the hypothalamus. He has developed a method of electrical stimulation of chosen points of the hypothalamus of the cat to study the behavior of the animal. By a series of slides of the hypothalamus, Professor Hess depicted a topographic map of the hypothalamus to localize the centers of the vegetative life. He has written many books, two of which are "Das Zwischenhirn: Syndrome, Localisationen, Funktionen" and "Die funktionnelle Organisation des Vegetativennervensystem." Workers who have adopted the new theories in neuropathology explained by Speransky (U.S.S.R.) based their research mostly on the studies of Professor Hess.

International Congress of Hematology in Montreux

The second meeting of the International European Society of Hematology took place in Montreux (Sept. 15-17, 1949) under the chairmanship of Professors Chevallier (Paris), Lambin (Louvain, Belgium) and Di Guglielmo (Napoli, Italy), with the cooperation of the International Society of Hematology, which was represented by its vice president, Prof. W. Dameshek (Boston), and the Swiss Society of Hematology, represented by its chairman, Dr. A. Alder.

Hemolytic anemias were discussed by Professor Dameshek, Professor Mallarme (France) and Professors Heilmeyer and Jung (Germany), who reviewed the congenital, acquired and toxic hemolytic anemias. The antimitotic substances were discussed by Professor Dustin (Belgium), Professor Haddow (Great Britain), Prof. L. M. Meyer (United States) and Professor Dameshek. Professor Dameshek reported the remissions he obtained in one third of his cases of leukemia.

French Congress of Medicine in Geneva

For the second time in its history, the Association des Médecins de Langue Française (Association of the Physicians of French Language) held its meeting in Geneva. This meeting lasted three days. The chairman was Prof. M. Roch, head of the Medical Clinic of the Geneva University; he is the well known author of the famous "Dialogues Cliniques." The meeting was organized by Prof. Eric Martin (Geneva), and about 400 physicians from different countries were present: France, Belgium, Luxembourg, Italy, Canada (Professor Lesage), Switzerland and also United States (Dr. Homburger). Interesting points of view were given on the following subjects: proteins of the plasma, hyperthyroidism and the treatment of cancer with hormones. On the last subject, Prof. A. Lacassagne (Paris), the world-renowned cancerologist, revealed that hypophysiectomy on the mouse stopped the development of cancer of the mammary gland.

A New Cancer Test

According to a recent publication by Menkes (*Médecine et Hygiène* 7: 369 [Nov. 15] 1949), the blood of cancer patients can destroy pentoses added to it. This "pentolytic" property was utilized in tests conducted on 176 subjects, of which 93 were cancerous, 63 noncancerous and 20 in good health. Pentolysis was negative for those apparently in good health, and positive in 110 of 120 tests on the cancerous subjects. Further confirmation of the diagnoses is being undertaken, and results of investigations on animals are to be published shortly.

ITALY

(From Our Regular Correspondent)

FLORENCE, Nov. 15, 1949.

Heart Disease and Pregnancy

Professor Colombi of Milan discussed heart disease and pregnancy at the Congress of the Italian Cardiologic Society in Stresa, which was attended by many Italian and foreign cardiologists and by many obstetricians. He said that the factors which determine an increased action of the heart during pregnancy are (1) the hormonal factor, because of changes of the endocrine glands resulting from conception and aggravated during pregnancy, labor and the postpartum period; (2) the metabolic factor, determined by the increase in organic combustion by the growth of the product of conception, and (3) the hemodynamic factor, in relation to the vascular anastomotic network in the placenta which presents characteristics equal to those of arteriovenous fistula. They constitute a shunt, which becomes established within the first two months, reaches its maximum of efficiency about the eighth month and is obliterated slowly in the last weeks preceding delivery. It is this arteriovenous fistula which determines the new orientation of scientists with respect to the dynamics of circulation during pregnancy.

Research carried out by the speaker and his co-workers indicated clearly that the heart during pregnancy is subjected to new hydrodynamic conditions by the variations of the amount of blood, by arterial dilatation and by the diminished peripheral resistance which induce an increased afflux of blood to the right side of the heart.

It is logical that these variations have more pronounced repercussions in women with heart disease. Those cardiac diseases in which the course is progressive present the major drawbacks in that pregnancy is tolerated badly or the disease becomes worse. There are some types of heart disease which may be tolerated well during pregnancy and delivery.

It is the duty of the cardiologist to evaluate the damage which might result from pregnancy with respect to the diseased heart. Study of the patient by the obstetrician and the cardiologist will allow them to determine the damage, to avoid grave episodes and to support the heart during gestation. It will also enable them to judge the advisability of an occasional interruption of pregnancy at the most suitable time and to institute the treatment required for a favorable course of pregnancy, which in a large number of cases may be a normal one without much inconvenience to the patient.

In the discussion which followed, it was emphasized that besides the arteriovenous fistula, present in all cases, there may be additional factors, not less important but perhaps more difficult to evaluate. There are those which determine the unexpected attacks of pulmonary edema and those which determine attacks for which the term of neurovegetative catastrophies was coined by Professor Condorelli. It is likely that one has to deal with humoral endocrine factors, partly of the type which may occur during premenstrual attacks, or with toxic factors.

Leptospirosis Icterohaemorrhagica

Several cases of leptospirosis icterohaemorrhagica treated with penicillin were reported at the Filippo Pacini Medical Academy of Pistoia. Professor Cantieri reported 10 cases in which the clinical diagnosis had been confirmed by serologic examination. The patients included only male subjects who had acquired the disease by working in marshes, rivers or sewers. They had nearly all the manifestations of meningism or of meningitis and icterus, sometimes associated with a severe typhoid state. Penicillin was administered in daily doses of 200,000 to 400,000 units with total doses of 400,000 to 2,200,000 units. In all cases the temperature was restored to normal and the meningitic signs disappeared rapidly. The icterus subsided slowly. There were no recurrences.

Dr. Bini of the Hospital of Pescia also treated several patients with penicillin, and all recovered in a short period. The recovery was more rapid when the patients were treated with penicillin during the first days of the disease, i. e., during the bacteremic, preicteric period. The penicillin has little effect on the icterus and on the hepatitis in cases of anicteric infection; the characteristic recurrent attacks of fever were no longer observed after the treatment.

Dr. Baldi reported that he obtained good results in 14 workmen with leptospirosis who worked in the marshes. Dr. Cosci reported on 30 patients; 15 of them were treated with bismuth preparations, sulfonamide compounds and aminopyrine; the disease was of eighteen days' duration, with temperature restored to normal by lysis, long convalescence, asthenia and anorexia. The remaining 15 patients were treated with 500,000 to 600,000 units of penicillin in twenty-four hours, with decrease in temperature and with remission of symptoms within the first twenty-four to forty-eight hours.

Correspondence

PROPOSED CANCER TEST

To the Editor:—Odell and his co-workers (*Science* **109**: 564, 1949; *Cancer Research* **9**: 362, 1949) of the University of Chicago recently reported that the vaginal fluid showed "consistently high values for beta-glucuronidase in the presence of untreated cervical cancer" and have proposed the assay of beta-glucuronidase in vaginal secretions as suited for large surveys of the population for detecting uterine cervical cancer. The selection of beta-glucuronidase as the enzyme for his study was stated to rest on the previous work of Fishman and his co-workers (*Cancer Research* **7**: 808, 1947), who found in the majority of cases studied enhanced beta-glucuronidase activity in human cancer tissue (breast, esophagus, stomach, colon, lymph nodes, uterus). The physiologic function of the enzyme is not well understood, although a relationship with the action of the estrogenic hormones has been investigated (Fishman, W. H., and Fishman, L. W.: *J. Biol. Chem.* **152**: 487, 1944).

Odell confirmed the presence of increased glucuronidase in cancer tissue (uterus) and reasoned, without experimental evidence, that the vaginal fluid in genital malignancy would become enriched with glucuronidase deriving from the tumor. In 20 assorted carcinomas of the genital tract (14 cervical cancers) high activity (over 320 units) of vaginal fluid glucuronidase was found "in every case." Of 73 patients with "benign" conditions, 14 (19 per cent) gave false positive reactions (values over 320), which were explained principally on the basis of pregnancy or the presence of Trichomonas vaginalis. Since these latter conditions can be recognized easily, the diagnosis of cancer of the cervix by the vaginal fluid glucuronidase would appear to be a matter of near certainty according to Odell's data and to the publicized reports in the nonmedical press.

Our experiences with this "diagnostic test" have proceeded to a point where a statement has become necessary. We have continued to observe the enrichment of cancer tissue with regard to beta-glucuronidase in uterine cervix, gastrointestinal tract and the like. However, with regard to vaginal fluid glucuronidase activity, 5 of 13 untreated carcinomas of the cervix showed values below 320 units. Of 428 nonpregnant controls of all ages, 130 (30 per cent) possessed values in excess of 320 units. In many of these cases values much higher than in the cancer group were encountered. Seventeen of the noncancer group with negative reactions and 14 of the group with false positive reactions had evidence of cervicitis and vaginitis (Trichomonas). Of the 130 subjects with conditions falling into Odell's category of malignant disease, none showed cytologic evidence by the Papanicolaou technic of uterine cancer, and in a number of these thorough clinical investigation did not reveal uterine cervical cancer. Moreover, in a few women with total hysterectomy showing no signs of vaginitis or cancer, values as high as 2,000 units have been obtained.

Although our evaluation of the vaginal fluid glucuronidase test is not yet complete, the high incidence of false negative and positive values we have encountered so far deserves the attention of others who may be using the test in the clinic for surveys. However, much more reliance may be placed on the glucuronidase activity of uterine cervical tissue as an indication of malignancy.

WILLIAM H. FISHMAN, PH.D.
S. CHARLES KASDON, M.D.
FREDDY HOMBURGER, M.D., Boston.

RECURRENT APHTHOUS ULCERS

To the Editor:—Virus causation of recurrent aphthous ulcers has not been proved. As recently as Oct. 1, 1949 (J. A. M. A. **141**: 362, 1949) and Sept. 24, 1949 (J. A. M. A. **141**: 299, 1949) in "Queries and Minor Notes" the consultants repeated the erroneous concept that this disease is caused by the virus of herpes simplex. In addition, one of the writers misquoted studies from this laboratory by indicating that there is significant alteration in antibody titer in patients with recurrent herpes simplex. We are taking this opportunity to correct these errors and to present a brief summary of our combined clinical and laboratory observations which are pertinent to the problem of recurrent ulcers of the mouth.

As part of a larger joint study of virus diseases of the skin by the departments of dermatology and pediatrics of the University of Pennsylvania at the Children's Hospital of Philadelphia, a number of patients have been studied with primary herpetic gingivostomatitis, recurrent herpes simplex and recurrent aphthous ulcers of the mouth. The investigation of a patient included a detailed history, smear and bacteriologic cultures of the ulcers, inoculation of material from the lesion into embryonated eggs or a rabbit's cornea, biopsy and serologic studies for herpes simplex antibodies in blood drawn during and after the acute episodes. The accompanying table is a summary of the pertinent findings in our patients, accumulated during the past three years.

Summary of Observations at the Children's Hospital of Philadelphia

	Recurrent Herpes Simplex of Skin (Lips, Face, Genitalia)	Recurrent Aphthous Ulcers	Primary Herpetic Gingivostomatitis
Number of cases	25	32	50
Herpes simplex virus isolated	Pos. (16/18)*	Neg. (0/27)	Pos. (28/35)
Specific inclusions in biopsy	Pos. (4/4)	Neg. (0/14)	Pos. (4/5)
Specific herpes simplex antibodies (neutralizing)	Present at onset; no rise in titer during convalescence (19/19)	Usually present at onset; no rise in titer during convalescence (8/13)	Absent at onset; rise in titer during convalescence (38/38)

* The numerator of the fraction indicates the number of patients with positive findings; the denominator indicates the number of patients in whom this test was performed.

In none of our patients with recurrent aphthae could we demonstrate the virus of herpes simplex by inoculation of embryonated eggs or by biopsy, methods which are regularly successful in known herpes simplex infections (Isolation of Herpes Simplex on the Chorioallantois, *J. Lab. & Clin. Med.* **34**: 402, 1949; Virus Diseases of the Skin, *Acta dermat. venereol.* **29**: 77, 1949; Acute Herpetic Gingivostomatitis in the Adult, *New England J. Med.* **241**: 330, 1949). In addition, no specific herpes simplex antibodies were present in the serums at the onset or during convalescence of 5 of the 13 patients with recurrent aphthous ulcers who were tested. This is in contrast to patients with proved herpes simplex lesions who invariably have specific antibodies at the onset of the disease or develop them during convalescence.

Two other laboratories have reported the results of their studies of recurrent aphthae to us. Dodd and Ruchman in Cincinnati (Recurrent Stomatitis, *J. Pediat.*, to be published)

and Jessner in New York City (personal communication) also failed to find laboratory evidence that the virus of herpes simplex causes recurrent aphthous ulcers. Several other theories have been proposed to explain recurrent aphthae, but in most patients the cause remains obscure.

HARVEY BLANK, M.D.
CARROLL F. BURGOON, M.D.
LEWIS L. CORIELL, M.D.
THOMAS F. McNAIR SCOTT, M.D.
Philadelphia 46.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS. *Part III.* Boston, Chicago and New York, January. *Parts I and II,* Feb. 13-15. Centers where there are approved medical schools and five or more candidates. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th Street, Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations, July 21. *Oral.* Philadelphia, April 23-27, Chicago, Oct. 8-11. Sec., Dr. Curtiss B. Hickcox, 745 Fifth Ave., New York 22.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various locations, Feb. 16. *Oral.* Washington, April 7-9. Sec., Dr. George M. Lewis, 66 East 66th Street, New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Chicago, Feb. 8-10. Boston, April 13-15. San Francisco, June 21-23. The oral examinations in the subspecialties will be held at the same time and places. Final date for filing applications for all examinations is Jan. 1. Asst. Sec., Dr. William A. Werrell, 1 West Main Street, Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, June 3. Sec., Dr. W. J. German, 789 Howard Ave., New Haven, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC. *Written and Reviews of Case Histories. Part I.* Various Centers. Feb. 3. *Oral Part II.* Atlantic City, May 21-28. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 1951. Final date for filing applications is July 1, 1950. *Practical.* Boston, May 22-26; Chicago, Oct. 2-6; West Coast, Jan. 1951. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY. *Part II,* New York City, Feb. 9-10. Sec. Treas., Dr. Harold A. Sofield, Room 1856, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* San Francisco, May. Chicago, October. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Richmond, Va., Feb. 10-12; Philadelphia, March 31-April 2; San Francisco, June 23-25. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral.* May-June. Sec., Dr. Louis T. Byars, 4647 Pershing Avenue, St. Louis, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH: *Oral and Clinical.* Chicago, Feb. 7-8. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe Street, Baltimore 5, Md.

AMERICAN BOARD OF PROCTOLOGY: *Parts I and II (Anorectal Surgery).* Chicago, Feb. 6-7. Secretary-General, Dr. Louis A. Buie, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Spring Examination. Date and location of examination to be announced later. Final date for filing applications is Feb. 1. Sec., Dr. F. J. Braceland, 102-110 Second Ave., S.W., Rochester, Minnesota.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Chicago, week of June 18. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: *Oral and Clinical.* Chicago, Feb. 11-15. Sec., Dr. Harry Culver, 7935 Sunnyside Road, Minneapolis 21.

BOARD OF THORACIC SURGERY: *Written.* Various locations. Jan. 16. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 27-29. Sec., Dr. D. G. Gill, 519 Dexter Avenue, Montgomery.

ALASKA: * Juneau, March 7. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARIZONA: * *Examination.* Phoenix, Jan. 17-18. *Reciprocity.* Phoenix, Jan. 21. Sec., Dr. J. H. Patterson, 316 W. McDowell Road, Phoenix.

ARKANSAS: * *Examination.* Little Rock, June 8-9. Sec., Dr. Joe Verser, Harrisburg. *Eclectic.* Little Rock, June 8-9. Sec., Dr. Clarence H. Young, 1415 Main Street, Little Rock.

CALIFORNIA: *Examination, Written.* Los Angeles, Feb. 27-March 2; San Francisco, June 19-22; Los Angeles, Aug. 21-24; Sacramento, Oct. 16-19. *Examination, Oral and Clinical, for Foreign Medical School Graduates.* Los Angeles, Feb. 26; San Francisco, June 18; Los Angeles, Aug. 20; San Francisco, Nov. 12. *Reciprocity, Oral Examination.* Los Angeles, Jan. 21; Los Angeles, Feb. 25; San Francisco, June 17; Los Angeles, Aug. 19; San Francisco, Nov. 11. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

CONNECTICUT: * *Examination.* Hartford, March 14-15. Secretary to the Board, Dr. Creighton Barker, 160 St. Ronan Street, New Haven. *Homeopathic.* Derby, March 9-10. Sec., Dr. Donald A. Davis, 38 Elizabeth Street, Derby.

FLORIDA: * Jacksonville, June 25-27. Sec., Dr. Frank D. Gray, 12 N. Rosalind Avenue, Orlando.

GEORGIA: *Examination.* Atlanta and Augusta, June. *Endorsement.* Atlanta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

GUAM: *Endorsement.* Agana, last Friday of each month. Sec., Capt. C. K. Youngkin, Dept. of Public Health, Guam, % F.P.O., San Francisco.

INDIANA: *Examination.* Indianapolis, June. Sec., Dr. Paul R. Tindall, 1138 K. of P. Bldg., Indianapolis.

IOWA: * *Examination.* Iowa City, June 12-14. Dr. Walter L. Bierring, Commissioner and Acting Director, Division of Licensure and Registration, State Department of Health, Des Moines.

MAINE: Portland, March 14-15. Sec., Dr. Adam P. Leighton, 192 State Street, Portland.

MASSACHUSETTS: *Examination.* Boston, March 14-17. Sec., Dr. George L. Schadt, 413 E. State House, Boston.

MINNESOTA: * Minneapolis, Jan. 17-19. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Building, St. Paul 2.

MISSOURI: *Examination.* Jefferson City, Feb. 9-11. *Reciprocity,* Feb. 4. Exec. Sec., Mr. John A. Hailey, Box 14, State Capitol Building, Jefferson City.

MONTANA: Helena, April 3-5. Sec., Dr. Otto G. Klein, First National Bank Building, Helena.

NEVADA: Carson City, May 1. Sec., Dr. George H. Ross, 112 Curry Street, Carson City.

NEW HAMPSHIRE: Concord, March 8-9. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 20-23. Sec., Dr. E. S. Hallinger, 28 West State Street, Trenton.

NEW MEXICO: * Santa Fe, April 10-11. Sec., Dr. Charles J. McGoey, Coronado Building, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 31-Feb. 3. Sec., Dr. Jacob L. Lochner, 23 S. Pearl Street, Albany 7.

NORTH CAROLINA: *Endorsement.* Raleigh, Jan. 23. Sec., Dr. Ivan Procter, 226 Hillsboro St., Raleigh.

OKLAHOMA: * *Examination.* Oklahoma City, June 7-8. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

PENNSYLVANIA: *Examination.* Philadelphia or Harrisburg, Jan. 23-25. Acting Sec., Mrs. Marguerite G. Steiner, 351 Education Building, Harrisburg.

PUERTO RICO: *Examination.* Santurce, March 7. Sec., Mr. Luis Cueto Coll, Box 3717, Santurce.

SOUTH CAROLINA: *Examination.* Columbia, June 26-29. *Reciprocity.* First Monday of each month. Sec., Dr. N. B. Heyward, 1329 Blanding Street, Columbia.

SOUTH DAKOTA: * Sioux Falls, Jan. 17. Sec., Dr. C. E. Sherwood, 300 First National Bank Building, Sioux Falls.

UTAH. *Examination.* Salt Lake City, June. Dir., Dr. Frank E. Lees, 324 State Capitol Building, Salt Lake City.

VIRGINIA: *Examination.* Richmond, June 23-24. *Endorsement.* Richmond, June 22. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

WASHINGTON: * Seattle, Jan. 23-25. Director, Department of Licenses. Mr. Edward C. Dohm, Olympia.

WYOMING: Cheyenne, Feb. 6. Sec., Dr. Franklin D. Yoder, State Capitol, Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: *Examination.* Little Rock, May 9. Sec., Mr. L. E. Gebauer, 1002 Donaghey Building, Little Rock.

CONNECTICUT: *Examination.* New Haven, Feb. 11. Address: State Board of Healing Arts, 110 Whitney Avenue, New Haven 10.

DISTRICT OF COLUMBIA: Washington, April 17-18. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Building, Washington.

FLORIDA: *Examination.* June 3. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.

OKLAHOMA: *Examination.* Oklahoma City, April 11. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

RHODE ISLAND: *Examination.* Providence, Feb. 8-9. Chief, Division of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Building, Providence.

TEXAS: *Examination.* Austin, Jan. 20-21 and April 21-22. Sec., Brother Raphael Wilson, 306 Nalle Building, Austin.

WASHINGTON. Seattle, Jan. 18-19. Sec., Department of Licenses, Mr. Edward C. Dohm, Olympia.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Naturopaths: Right to Enjoin Enforcement of Medical Practice Act.—This was an action for a declaratory judgment to have portions of the medical practice act of New Jersey adjudged unconstitutional and, in addition, to recover pecuniary damages from certain of the defendants for alleged violation of the civil rights act. The case was heard in the United States district court for the district of New Jersey.

The plaintiffs are the American Association for Oxygen-Therapy, Incorporated, and a number of individual naturopaths, and the defendants are members of the New Jersey State Board of Medical Examiners and certain personnel of the Attorney General's office. The present proceedings related to the plaintiff's motions for a temporary restraining order to stay court actions and to convoke a statutory three judge court to secure an interlocutory injunction.

The plaintiff Blass alleged that he developed a system of curative processes whereby a combination of nonpoisonous natural products, beneficial to the human body, eliminated and removed all diseases and ill health from it and that he assigned the secret formulas for the system to the plaintiff corporation for marketing purposes. He claimed to be a graduate naturopath and said that his profession did not employ surgery or processes common to allopathic and homeopathic practitioners but treated diseased bodies by natural means. He was arrested on a warrant, tried and convicted in a quasicriminal action by a state court for violations of the New Jersey medical practice act, but he asserted that after his arrest he was denied the right to communicate with counsel and the right to be informed of the nature and details of the accusation against him until he posted security and that after posting bail he was refused a bill of particulars of the accusation against him and trial by jury. He claimed that the evidence presented against him, secured by professional and anonymous witnesses who called at his place of business, together with the evidence presented on his own behalf, clearly proved that he practiced nothing remotely touching medicine and surgery. He contended that confusion and doubts have arisen because of numerous rulings by the state courts concerning what constitutes the practice of medicine by naturopaths. There were additional allegations that the statute confers monopoly on physicians and surgeons, that the medical practice act is unconstitutional and that the defendants have unlawfully discriminated against the plaintiffs in favor of allopathic and homeopathic practitioners.

In consideration of the request for the convening of a three judge court, the district court said that if the complaint shows that the question "is obviously without merit or because its unsoundness so clearly results from the previous decisions of this court as to foreclose the subject and leave no room for the inference that the question sought to be raised can be the subject of controversy . . ." a federal court is without jurisdiction to convene a three judge court. A long line of decisions have upheld the right of a state to regulate the practice of medicine and the allied professions; to designate, limit or restrict what shall constitute the practice of medicine and the allied sciences; to authorize an administrative agency to provide for the regulation of the practice of medicine and the allied sciences; and to enforce either the statutes of the state or regulations of the administrative agency. No jurisdiction exists, therefore, for invoking the procedure requested by the plaintiffs.

There remain, said the court, those allegations pertaining to alleged violations of the civil rights act, wherein the defendants were alleged to have violated Article IV, section 2 and the First, Fifth, Sixth, Seventh, Thirteenth and Fourteenth amendments to the United States Constitution. The allegations of plaintiff Blass concerning Article IV, section 2 and the Fifth, Sixth, Seventh and Thirteenth amendments fail to state a cause of action.

The allegations concerning the First Amendment, said the court, are based on the plaintiff's contention that the acts of the defendants in enforcing the medical practice act prevented him from disseminating information concerning the science of naturopathy. To constitute a violation over which this court is required to exercise jurisdiction, the acts of state officials must have been in violation of federal law. The alleged violation of the First Amendment was based on the fact that in prosecuting the violation of the medical practice act, plaintiff Blass was silenced by the in torrorem effect of the state action. Unless the defendants acted outside the limits of the authority vested in them by law, no violation of a federal right has occurred.

The state of New Jersey has provided for a comprehensive scheme whereby the practice of medicine is regulated by the State Board of Medical Examiners. Plaintiff Blass was accused of having violated these regulations and statutes, and, in conformity to the procedure provided in the act, suit was instituted against him. He complained that the information under which he was tried failed to inform him as to the nature of the offense, that he was denied this information on his demand for a bill of particulars and that the information on which his accusation and conviction was based was obtained by anonymous and professional informants. No appeal was taken from the action of the trial court to the appellate courts of New Jersey whereby any alleged invalidity in the accusation, trial and judgment could have been tested to determine whether errors had been committed under the then current New Jersey practice. Rather, said the district court, he has filed this complaint seeking to enjoin the enforcement of a state court judgment and in essence has sought to convert this court into an appellate forum to pass on matters of state court trial procedure. It is a familiar rule of law, continued the court, that courts of equity do not ordinarily restrain criminal prosecutions. There is a complete failure on the part of the plaintiff to show in his complaint that the defendants performed any act involving him other than those required of them by the medical practice act of the state or that they violated under color of state law any right secured for him by the federal constitution. Accordingly the district court concluded that the plaintiff was not entitled to relief by way of either injunction or damages against the defendants and his complaint was therefore dismissed.—*Blass et al. v. Weigel et al., 85 F. Supp. 775 (N. J., 1949).*

Medical Motion Pictures

FILM REVIEW

Kidneys, Ureters and Bladder. Their Structure and Function. 16 mm., black and white, sound, showing time ten minutes. Produced in 1947 by and procurable on rental or purchase from The Bray Studios, Inc., 729 Seventh Avenue, New York.

This motion picture clearly illustrates the important anatomic features and the functioning of the kidneys, the ureters and the urinary bladder. Animated drawings depict the functioning relationships of the constituent parts of the system and also the process of urine formation and the elimination of waste matter. The value of the film would have been increased if it demonstrated the opening and closing of the sphincter muscle from the outlet of the bladder. This film is recommended for showing to high school and college classes in hygiene, health and biology as well as to classes in nursing education. The photography, animation and narration in this motion picture are well done.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in Continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1938 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

78:141-294 (Aug.) 1949

*Value of Biopsy of Liver in Nutritional Dystrophy: Evaluation of Treatment with Choline and Dried Stomach. J. Meneghello, J. Espinoza and L. Coronel.—p. 141.
*Disseminated Visceral Lesions Associated with Extreme Eosinophilia: Pathologic and Clinical Observations on Syndrome of Young Children. W. W. Zuelzer and L. Apt.—p. 153.
Rubella-Deafened Infants: Comparison of Group of Rubella-Deafened Children with a Group of Hereditarily Deaf Children and Their Sibs. L. A. Hopkins.—p. 182.
Streptomycin in Treatment of Whooping Cough. L. W. Wannamaker, J. L. Kohn and M. Weichsel.—p. 201.
*Further Studies on Use of Streptomycin in Treatment of Whooping Cough. K. S. Shepard, J. L. Kohn, S. R. Kaplan and T. C. Allen.—p. 212.
Spread of Diarrhea of Unknown Origin in a Ward for Infants. J. J. Shields.—p. 217.
Hereditary Factors in Infantile Progressive Muscular Atrophy: Study of One Hundred and Twelve Cases in Seventy Families. S. Brandt.—p. 226.
Peritoneal Irrigation: Method of Treatment of Acute Renal Failure in an Infant. W. R. Buerger, E. C. Lambert and B. A. Maitland.—p. 237.
Cushing's Syndrome Due to Tumor of Adrenal Cortex: Report of Case of an Eleven Month Old Infant, with Apparent Operative Cure. H. M. Goldstein.—p. 260.

Biopsy of Liver in Nutritional Dystrophy.—Meneghello and his associates of Santiago, Chile, report on liver biopsies in infants with nutritional dystrophy. The syndrome is known under various terms in different South American countries. In the United States it is usually designated as nutritional edema or hydropigenous multideficiency dystrophy. The authors studied 31 patients between 4 and 30.5 months of age, the average age being 14.6 months. These patients were distributed in three groups according to the treatment they received. Eleven infants of group A were treated with complete alimentation and additional dried stomach U.S.P., prescribed in doses of 10 grains (0.65 Gm.) daily, diluted in 100 cc. of distilled water, plus 5 cc. of tenth-normal hydrochloric acid. This mixture has a disagreeable taste, and many patients refused it. The dried stomach was administered for four to ten days. Group B comprised 14 patients, to whom, besides complete alimentation, choline chloride in juice was given. The dose was 5 grains (0.32 Gm.) daily for periods determined by the degree of control of the fatty degeneration of the liver seen on biopsy. Group C consisted of 6 patients serving as controls and treated only with complete alimentation. The examination included blood cell count, blood sugar and cholesterol determination and hepatic function tests (the Takata-Ara, Hanger and prothrombin tests). As a rule, these tests were repeated after two weeks, together with the biopsy, for which the authors used the Silverman needle by the abdominal approach. A total of 89 liver biopsies were made on 29 patients. Intense hepatic fatty degeneration was proved consistently. The clinical evolution depends in great part on the relation between the condition of the patient and the degree of hepatic damage. Clinical improvement generally precedes the regression of the hepatic lesions. No difference in the clinical course of hepatic improvement was observed among patients treated with dried stomach, choline and all-inclusive alimentation. No parallelism appears to exist between the functional involvement and the intensity of the hepatic damage.

Visceral Lesions With Eosinophilia in Young Children.—Zuelzer and Apt point out that among the conditions associated with pronounced and persistent eosinophilia of the blood there is an obscure group of disorders reported under various names, such as chronic eosinophilia, eosinophilia leukemoides, eosinophilia and splenomegaly, Loeffler's syndrome and others. Prompted by a chance observation made in the course of an autopsy, the authors studied biopsy speciments of liver obtained from patients with excessive eosinophilia and observed a characteristic widespread lesion which seems to represent the anatomic substrate of a clinical entity. The cases were characterized by eosinophilia of the blood and bone marrow, hyperleukocytosis and hyperglobulinemia persisting over long periods in children ranging in age from 18 months to 3 years and presenting variable clinical pictures. Among the manifestations were hepatomegaly, pulmonary infiltrations, asthmatic complaints, joint symptoms, urticaria and convulsions. Through much of their course, however, the majority of the patients were free of symptoms. The essential unity of the conditions is based on the character of the pathologic lesions, demonstrated by biopsy specimens or at necropsy, in the liver in 4 cases. The lesions consisted of necrosis, granuloma formation and severe eosinophilic infiltration and corresponded to those described by other authors in the lungs of patients with the so-called Loeffler syndrome. They are interpreted as the expression of a common pathologic process of variable localization and severity, the nature of which is regarded as an allergic-hyperergic tissue response to undetermined antigens. In contrast to the picture of Loeffler's syndrome in adults, with eosinophilia and leukocytosis of usually moderate degree and with predominantly pulmonary localization, the process in young children is likely to affect the liver and tends to be associated with a greater distortion in the blood picture. Loeffler's syndrome may be regarded as a special case of pulmonary involvement in a broad range of allergic phenomena. The clinical picture depends on the organs involved and on the severity of the process. The entity appears to be common. Differentiation of these cases from cases of leukemia is necessary. The condition appears to be benign and self limited, though often of long duration.

Streptomycin in Whooping Cough.—Shepard and his co-workers review observations on 64 children who were treated with streptomycin. Forty-three of the children were less than 3 years old; the others were older. In the children under 3 years of age, the streptomycin was administered simultaneously by aerosol route and intramuscular injection. In children over 3 years of age the streptomycin was given by aerosol only. The authors believe that streptomycin had a favorable influence on the course of whooping cough in children under 1 year of age. The clinical course was not so favorable in children over 1 year of age. There seems to be no advantage in the combined administration of streptomycin by aerosol route and intramuscular injection when compared with either aerosol or intramuscular injection alone.

American Journal of Hygiene, Baltimore

50:1-142 (July) 1949

Effect of Removal of Adhering Tissue Fluid Upon Growth and Survival of Embryonic Tissue in Vitro. L. L. Layton and H. Tutelman.—p. 1.
Demyelinating Encephalomyelitis in Dog Associated with Antirabies Vaccination. G. A. Jervis, R. L. Burkhart and H. Koprowski.—p. 14.
Japanese Equine Encephalomyelitis: 1947 Epizootic. II. Serological and Etiological Studies. K. F. Burns, W. D. Tigertt and M. Matumoto.—p. 27.
Experimental Transmission of Japanese B Encephalitis Virus by Culex Tritaeniorhynchus and Culex Pipiens Var. Pallens, Suspected Natural Vectors. W. McD. Hammon, D. M. Rees, J. Casals and G. Meiklejohn.—p. 46.
Isolations of Japanese B Encephalitis Virus from Naturally Infected Culex Tritaeniorhynchus Collected in Japan. W. McD. Hammon, W. D. Tigertt, G. Sather and H. Schenker.—p. 51.
*Poliomyelitis Attack Rates in American Troops, 1940-1948. J. R. Paul.—p. 57.
Chloramphenicol (Chloromycetin) in Chemoprophylaxis of Scrub Typhus (Tsutsugamushi Disease): Epidemiological Observations on Hyperendemic Areas of Scrub Typhus in Malaya. C. B. Philip, R. Traub and J. E. Smadel.—p. 63.
Id.: II. Results with Volunteers Exposed in Hyperendemic Areas of Scrub Typhus. J. E. Smadel, R. Traub, H. L. Ley Jr. and others—p. 75.
Studies on Chemotherapy of Filariasis. G. F. Otto and T. H. Maren.—p. 92.

Poliomyelitis Incidence in American Troops.—Paul shows that the rates at which United States troops contracted poliomyelitis during the years 1943 to 1948 were different in different parts of the world. They were higher in the Far East and Philippine Islands than elsewhere. As one explanation of

this fact the author suggests that it is likely that there is a large amount of poliomyelitis virus (perhaps representing a variety of strains) in areas where previously poliomyelitis had been considered as rare. Furthermore, it is likely that clinical poliomyelitis may be much more prevalent in some areas, including tropical or semitropical areas, than had previously been supposed. This impression has been recently substantiated by dispensary and hospital surveys in Palestine and Egypt and by a review of mortality statistics in Japan. In these areas, because the acute disease has been largely limited to sporadic cases in young infants, large epidemics have seldom been reported and nonparalytic cases in natives have practically never been reported, there is an erroneous impression that both the virus and the disease are rare. In such areas the clinical disease has come quickly to the surface when immigrant troops arrive. Much more research work is necessary before an adequate explanation of these phenomena can be expected.

American Journal of Medical Sciences, Philadelphia

218:121-240 (Aug.) 1949

Absorption of Gold from Pellets of Gold Salts (Aurothioglycolanilide) Implanted Subcutaneously and Intramuscularly: Its Application in Treatment of 6 Cases of Rheumatoid Arthritis. H. M. Margolis, G. H. Fetterman and P. S. Caplan.—p. 121.
*Treatment of Pneumonia and Other Infections with Soluble Sulfonamide, Gantrosan (NU-445; 3,4-Dimethyl-5-Sulfanilamido-Isoxazole). R. L. Brickhouse, M. H. Lepper, T. E. Stone and H. F. Dowling.—p. 133.
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Value of Liver Function Tests in General Hospital Practice. C. Moses.—p. 194.
*Studies in Pernicious Anemia Patients Treated with Liver Extract and Folic Acid Antagonists. L. M. Meyer, N. D. Ritz, A. Caccese and others.—p. 197.
Pain Reaction Threshold in the Menopausal Syndrome. R. F. Schilling and M. J. Musser.—p. 204.
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Recurrent Migrainoid Headaches Associated with Spontaneous Hypoglycemia. C. F. Wilkinson Jr.—p. 209.
Pericardial and Cardiac Surgery. H. M. Smathers.—p. 213.
Ocular Fundi in Relation to Operations for Hypertensive Cardiovascular Disease. R. W. Hollenhorst and H. P. Wagener.—p. 225.

Treatment of Various Infections with Gantrisin®.—Brickhouse and co-workers treated 142 patients with various infections, with gantrisin® (3, 4-dimethyl-5-sulfanilamido-isoxazole)—previously gantrosan—a new sulfonamide compound which is more soluble at various levels of p_H than the sulfonamide compounds in general use. The drug is available in 0.5 Gm. tablets for treatment by mouth and in 10 cc. ampuls containing 1 Gm. of the lithium salt for intravenous, subcutaneous or intramuscular administration. An initial dose of 6 Gm. followed by 1 Gm. every four hours was given for most infections. For urinary infections 2 Gm. were given initially with 1 Gm. every four hours thereafter. Comatose patients were given 6 Gm. intravenously followed by 3 Gm. by subcutaneous injection every eight hours until they could be given the usual oral dose. Children were given doses proportionate to their ages on the basis of 0.06 Gm. per pound of body weight for each twenty-four hour period, half the twenty-four hour dose being given as the initial dose. One hundred and twenty patients recovered; treatment failed in 19, and 3 died. Therapeutic results in pneumococcic pneumonia, meningococcic meningitis and various urinary infections caused by gram-negative rods were similar to those observed with the use of sulfadiazine or sulfamerazine. Urinary complications were limited to gross hematuria in 1 patient. Crystals were observed in the urine of 1 other patient. Dermatitis or fever attributed to the drug was observed in 5 patients. Nausea occurred in 4 patients and vomiting in none. The striking difference between this drug and the other sulfonamide compounds, with the exception of sulfanilamide, is the infrequency of crystalluria and the almost complete absence of renal complications. Gantrisin® is recommended for use when a sulfonamide compound is required in a patient in whom renal complications must be particularly guarded against.

Liver Extract and Folic Acid Antagonists in Pernicious Anemia.—Meyer and co-workers administered synthetic folic acid inhibitors to 5 patients—3 men between the ages of 50 and 76 and 2 women aged 64 and 81—with pernicious anemia treated with adequate doses of liver extract. In case 1, 200 mg. of methyl pteroic acid resulted in no reticulocyte response and a stationary blood picture for one month. After discontinuance of methyl pteroic acid the further administration of liver extract was followed by a slow rise in hemoglobin and red cells, but no reticulocyte response occurred. In case 2, adequate liver therapy and 60 mg. of antagonist per day were followed by no change in reticulocytes or peripheral blood cell count. After methyl pteroic acid was discontinued and repeated liver extract injections were given, there was a slow rise in the red cells and hemoglobin, but no reticulocyte response was evoked. The third patient had a similar course. The fourth patient came under observation after a satisfactory reticulocyte count had been attained. The administration of 200 mg. of methyl pteroic acid for sixteen days had no apparent effect on the reticulocytes, but the hemoglobin and red cell count remained unchanged. The blood cell count was stationary fifteen days after the drug was discontinued and then began to rise slowly. The fifth patient was treated with pteroyl aspartic acid, a less potent folic acid antagonist than methyl pteroic acid. Although a satisfactory reticulocyte response occurred after administration of 10 units of liver extract, no change in hemoglobin and red cells took place. The second, third and fourth patients showed pronounced megaloblastosis after treatment with the folic acid antagonists, even with adequate liver therapy. All the patients appeared ill and complained of weakness, fatigue and somnolence while receiving either antagonist. The lack of hematologic response in patients with pernicious anemia treated with adequate doses of liver extract and a folic acid antagonist suggests that pteroyl glutamic acid is necessary for the production of red blood cells. One additional patient with pernicious anemia in relapse was treated simultaneously with methyl pteroic acid, vitamin B_{12} and 4-amino 10-methyl pteroyl glutamic acid. There was no clinical remission or reticulocyte response, and the hemoglobin, red cell and white cell counts did not increase.

Archives of Dermatology and Syphilology, Chicago

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*Treatment of Early Syphilis with Penicillin: Report on Three Hundred and Twenty-Four Patients Treated with 1,200,000 Units Over Seven and One-Half Days. R. L. Barton, T. J. Bauer, R. M. Craig and G. X. Schwemlein.—p. 150.
Concurrent Melanosis and Hypertrichosis in Distribution of Nevus Unius Lateris. S. W. Becker.—p. 155.
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*Tropical Anhidrotic Asthenia: Thermogenic Anhidrosis. E. C. Fox.—p. 173.
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*Pemphigus Erythematosus. F. E. Senear and L. B. Kingery.—p. 238.
Treatment of Early Syphilis with Penicillin G: Administration of Penicillin G in Peanut Oil and Wax Twice Weekly for Eight Weeks. L. W. Shaffer and C. J. Courville.—p. 253.
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Epithelioma: Clinical and Histologic Data on 1,025 Lesions. D. G. Welton, J. A. Elliott and P. Kimmelstiel.—p. 277.
Nodular Vasculitis. A. R. Woodburne and O. S. Philpott.—p. 294.
Therapy of Psychosomatic Dermatoses. C. S. Wright.—p. 303.

Penicillin in Early Syphilis.—Barton and co-workers treated 324 patients with early syphilis with penicillin. There were 176 male and 148 female patients; 66 were white and 258 were Negro. An aqueous solution of sodium penicillin was administered intramuscularly every three hours, 20,000 units per injection, for a total of sixty injections or 1,200,000 units of the drug. The period of treatment extended over seven and

one-half days. Treatment failed in 60 of these patients during a minimum observation period of eighteen months. There were 3 patients with relapsing primary syphilis, 7 with primary syphilis progressing to secondary syphilis, 21 with relapsing secondary syphilis and 29 with serologic relapse. The over-all cumulative failure rate, disregarding the stage of the disease, was 29.6 per cent at the end of one year's observation.

Tropical Anhidrotic Asthenia.—Fox reports 4 cases of a new syndrome, thermogenic anhidrosis, the patients presenting a typical history and classic symptoms of the condition. A period of excessive sweating and some degree of prickly heat was followed by cessation of sweating of the entire body below the neck, with an outpouring of sweat from the face and neck. From the neck down, the skin was warm and dry. There was generalized weakness, exhaustion, sensation of body warmth, dizziness, headache, palpitation and rapid respiration, developing during the heat of the day and on exertion. Three of the patients made a complete recovery over a period of three to five weeks with rest in a cool environment. A review of the literature indicates that the condition has been observed throughout the civilized world. The significant process is a defect of keratinization with the production of hyperkeratotic plugs which obstruct the sweat gland ducts. The systemic manifestations occur as a result of changes in thermoregulation, with attempts at dissipation of heat by increased respiration. Some fundamental pathologic process of systemic origin must produce this syndrome, but it is probably unrelated to control of sweating by either the central or the peripheral nervous system. The condition probably represents a systemic disturbance which interferes with keratinization, related to enzymes, vitamins or some other physiologic factor.

Pemphigus Erythematosus.—Senear and Kingery believe that cases which present the combination of elements suggesting features of lupus erythematosus, seborrheic dermatitis and pemphigus will in most instances prove to be of pemphigus erythematodes. The histologic picture of lupus erythematosus should exclude the case from the category of pemphigus erythematosus. In some cases the lupus-erythematosus-like element may predominate, in others the seborrheic and in still others the pemphigoid. It is apparent that these varied elements are all part of one basic process. Manifestations closely simulating lupus erythematosus, seborrheic dermatitis and even psoriasis, impetigo and eczema may occur in different cases or at different periods in the same case. Although originally it was thought that pemphigus erythematodes was a benign type, experience has shown that a fatal outcome is not uncommon, when the clinical picture has changed to that of pemphigus vulgaris or pemphigus foliaceus. In exceptional instances pemphigus erythematosus may develop subsequent to, rather than preceding, the vulgaris or foliaceus type of pemphigus. With the acceptance of this disorder as a form of pemphigus and not as an entity, there is no justification for the retention of the designation "Senear-Usher syndrome." The term pemphigus erythematodes, as originally suggested by Ormsby, seems to the authors to be the most suitable.

Archives of Neurology and Psychiatry, Chicago

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Effects of Ultraviolet Radiation on Exposed Brain. A. R. Elvidge and A. A. Morris.—p. 127.
Electroencephalographic Changes After Prefrontal Lobotomy with Particular Reference to Effect of Lobotomy on Sleep Spindles. M. A. Lennox and J. Coolidge.—p. 150.
Phobic Syndrome: Study of 86 Patients with Phobic Reactions. W. B. Terhune.—p. 162.
Comparison of Adjunct Group Therapy with Individual Psychotherapy. R. E. Peck.—p. 173.
*Role of Repeated Trauma by Pneumatic Drill in Production of Amyotrophic Lateral Sclerosis. B. J. Alpers and R. A. Farmer.—p. 178.
Observations on "Major" and "Minor" Causalgia. F. Echlin, F. M. Owens Jr. and W. L. Wells.—p. 183.
Studies on Occipital Lobe: I. Significance of Small Areas of Preserved Central Vision. G. M. Austin Jr., F. H. Lewey and F. C. Grant.—p. 204.
Allesthesia and Disturbance of Body Scheme. M. B. Bender, M. F. Shapiro and H. L. Teuber.—p. 222.

Repeated Trauma by Pneumatic Drill and Amyotrophic Lateral Sclerosis.—Experience with 2 patients in whom symptoms of amyotrophic lateral sclerosis followed the use of a pneumatic drill raised the question of whether repeated trauma might play a role in the precipitation of the disease. A man, aged 63, who had worked with a pneumatic hand drill for nine months, showed symptoms in the eighth month of its use. There were signs of anterior horn cell disease confined largely to the cervical portion of the spinal cord. A man who had worked for over three years with a pneumatic drill showed pronounced anterior horn cell disease in the cervical region and elsewhere. Whether the repeated hammering of a pneumatic drill in these cases was sufficient to produce the amyotrophic syndrome is not certain. If such a connection could be demonstrated, it would certainly be applicable to relatively few cases, since many instances of amyotrophic lateral sclerosis develop without exposure to such hazards. It seems possible that repeated concussions could be transmitted to the spinal cord to produce changes in susceptible anterior horn cells. The authors cite Hassin's observation of the picture of amyotrophic lateral sclerosis after spinal cord concussion and animal experiments carried out by several investigators. They also mention the occurrence of vasospastic phenomena in the hands of workers with pneumatic hammers. The rapid percussion in the pneumatic hammers presumably sensitizes the digital vessels so that Raynaud symptoms occur. Though no observations are available on the effect of such percussion on the vessels of the spinal cord, it seems not unreasonable to assume that they may occur in the use of pneumatic drills supported against the shoulder.

Archives of Physical Medicine, Chicago

30:495-546 (Aug.) 1949

Electromyographic Diagnosis of Lower Motor Neuron Disease. J. G. Golseth and O. L. Huddleston.—p. 495.
Influence of Atropine on Effects of Mecholyl Ion Transfer on Peripheral Circulation in Man. J. W. Gersten, K. G. Wakim, G. M. Martin and F. H. Krusen.—p. 501.
Physical Medicine in Amputations. F. W. Hark.—p. 511.
Efficacy of Peripheral-Acting Drugs in Treatment of Experimental Spasticity. N. M. Hajek and H. M. Hines.—p. 517.
*Colonic Irrigation. C. O. Molander.—p. 523.
Possibilities of Hydrotherapy in Psychiatric Hospital. P. A. Nelson and D. J. Erickson.—p. 526.

Colonic Irrigation.—The ordinary enema is given with the purpose of inducing defecation, whereas irrigation is used to wash out material situated above the defecation area and to lavage the wall of the bowels as high as the water can be made to reach. Irrigation requires that the fecal mass in the lower colon shall have been expelled and that the liquid shall be passed into the colon so gently that it does not arouse the defecation reflexes. Molander and his colleagues at the Michael Reese Hospital use colonic irrigation for cleansing, for assisting in diagnosis and for corrective procedures. For cleansing they remove fecal impactions and wash the colon before operation for cancer or other tumor masses in the rectum or intestinal tract. They cleanse and wash the intestinal loop prior to closure of an ileostomy, colostomy or sigmoidostomy, and they cleanse the intestinal tract of a barium enema. Irrigation is done for diagnostic purposes to enable the referring physician to make a better rectal examination and to enable the roentgenologist to get clearer pictures of the bladder and colon. Fecal specimens may be obtained for laboratory study at any stage of the irrigation. The objective of corrective therapy is to produce a state of tonicity in the musculature of the large intestine whereby the patient will defecate normally. Contraindications to colonic irrigations are: loose sphincter, painful hemorrhoids or fistula, debilitation, numerous polypi, tuberculosis, rectal infections, painful skin lesions around the anal opening, syphilis, massive carcinoma or other malignant tumors making it impossible to insert a rectal tube, and severe diverticulitis. Before giving an irrigation, the physiatrist must understand the indications, the contraindications, the technics involved and the purpose of the irrigation. He should be familiar with the diagnosis and history of the case and should make an examination to detect possible contraindications. Experience in correct irrigation procedures is important, and the apparatus should be of the pressure and vacuum gage variety. Fifteen years of experience has taught the author that there is a place for colonic irrigation in a large general hospital, but the indications for its use are limited and contraindications are numerous.

Bulletin New York Academy of Medicine, New York

25:403-470 (July) 1949

Iron Metabolism and Hemochromatosis. S. Granick.—p. 403.
Present Status of Vitamin B_{12} in Pernicious Anemia. E. H. Reisner Jr. —p. 429.
Pain in Lumbosacral Region. J. Browder.—p. 434.

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Allergy and Antihistamine Therapy: Review. M. H. Loveless and M. Dworin.—p. 473.
Medical and Surgical Treatment of Peptic Ulcer. C. M. Jones.—p. 488.
Modern Treatment of Syphilis, Including Syphilis of the Central Nervous System. E. W. Thomas.—p. 505.
Rise and Progress of Medical Education in Scotland. D. Guthrie.—p. 521.

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30:357-410 (July) 1949

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30:411-474 (Aug.) 1949

SYMPOSIUM ON THE SCHIZOPHRENIAS

Dementia Praecox as Described by Kraepelin. C. McIntyre.—p. 412.
Schizophrenia as Described by Bleuler. C. A. Mangham.—p. 414.
Jung's Views on Dementia Praecox. D. Jordan.—p. 416.
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Meyerian Conception of Dementia Praecox. M. Mathews.—p. 420.
Contributions of Harry Stack Sullivan to the Understanding of Schizophrenic Patients. J. Higgins.—p. 422.
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Biology of Schizophrenia. I. H. Weiland.—p. 426.
Nature of Schizophrenias Suggested by Modern Psychotherapists. J. Paras.—p. 428.

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Drainage, Streptomycin and Tuberculosis. B. L. Brock.—p. 129.
Physiological Significance of Bronchiectasis. D. Carr, E. F. Skinner, W. E. Denman and C. R. Kessler.—p. 137.
*Adenoma and Cylindroma of Bronchus. W. Van Hazel, P. H. Holinger and R. J. Jensik.—p. 146.
Biochemical Studies in Cancer Diagnosis. M. M. Black.—p. 169.
Acute Fatal Asphyxia Due to Aortic Aneurysm in Patient with Four Saccular Aneurysms of Thoracic Aorta: Case Report. G. S. Barnet and A. S. Glushien.—p. 177.
*Chronic Bilateral Basal Pulmonary Fibrosis. B. E. Goodrich and T. D. Johnson.—p. 184.
Basal Tuberculosis Simulating Sub-Phrenic Abscess. R. J. Gross and F. H. Schaefer.—p. 193.
Surgical Therapy of Pulmonary Tuberculosis at Veterans Administration Chest Center. R. Friedlander and W. M. Chardack.—p. 197.
Stomatitis and Dermatophytosis Coincident to Streptomycin Therapy. J. C. Mulhern.—p. 214.
Hydrothorax, Ascites, and Pelvic Endometriosis: Report of Case. H. C. Stearns and J. E. Tuhy.—p. 220.
Tuberculosis Control in Ohio State Reformatory. O. A. Beatty and J. V. Horst.—p. 225.
Tuberculosis Among Indians of the United States. A. Reifel.—p. 234.

Adenoma and Cylindroma of Bronchus.—Van Hazel and his associates present observations on 20 cases of adenoma and 2 of cylindroma that have been seen during the past twelve years. The adenomas are considered as extremely slowly growing but invasive tumors, rather than metastasizing malignant neoplasms, whereas cylindromas meet all the criteria of malignant lesions. Choice of therapy was influenced by the location and histologic character of the lesion, the presence or absence of bronchopulmonary changes peripheral to the lesion, the degree of hemorrhage associated with the bronchoscopic procedures and the response to endobronchial therapy. Of the 20 patients with adenoma, 10 were treated by bronchoscopy alone and 10 by subsequent surgical procedures. In the bronchoscopic group complete removal was effected in 5, of whom 4 were improved, and 1 was seen for biopsy only. In the surgical group, total pneumonectomy was performed in 6 cases; at the time of reporting 4 of these were living and well and 1 was improved; 1 had died postoperatively. Lobectomy was performed in 3 cases; 1 of these was living and well, 1 improved and 1 died postoperatively. The tenth surgically treated patient had a thoracotomy with cautery drainage, resection being impossible because of extensive adhesions. In the cylindroma group, 1 patient was treated bronchoscopically for five and a half years merely to keep the tracheal and bronchial airway open since the tumor had involved the entire right bronchus and invaded the trachea at the time of diagnosis. The second patient was treated by immediate pneumonectomy but had a recurrence five and a half years later.

Chronic Bilateral Basal Pulmonary Fibrosis.—Goodrich and Johnson apply the term chronic bilateral basal pulmonary fibrosis to a condition characterized by chronic cough, moist rales at the lung bases and basal pulmonary infiltration. Ninety-nine patients with chronic bilateral basal pulmonary fibrosis have been observed. Methods of evaluation included electrocardiograms, studies on the venous pressure and circulation time, bronchoscopy, studies of the vital capacity and sputum examinations with cultures and animal inoculations. Treatment was given for congestive heart failure. Chemotherapy and antibiotics were employed. Drugs and desensitization to foreign proteins were used to control allergy. Cough, bilateral moist rales and basal fibrosis were associated with specific causes in 81 of the 99 patients. Obscure congestive heart failure was frequently present. Bronchiectasis, pulmonary emphysema or bronchial asthma were likewise frequently associated with repeated episodes of infection and the production of chronic basal infiltration. Less frequently, in lymphogenous dissemination of silent gastric carcinoma there was for a period a pulmonary state of the type under study. In rare cases of infiltrative primary pulmonary malignancy, similar findings were temporarily present. Sarcoidosis was confusing in some instances. Various pneumonoconioses were accompanied with basal abnormalities. In 3 instances the pulmonary infection and fibrosis associated with cystic disease of the pancreas occurred chiefly in the lower portions of the lungs. In rare instances pulmonary arteriosclerosis was considered responsible. In postradiation fibrosis also there were bilateral basal infiltration and moist rales. No definite etiologic factors were discovered in the remaining 18 of the 99 cases. Lesions casting similar shadows may be quite different when microscopically examined. With failure of the self-cleansing mechanism of the lung, fibroblastic proliferation can occur whether the substance retained is congestive or infectious in nature, metabolic in origin or derived from inhaled particles. Age, with its increased tissue vulnerability, may play a part in this disorder.

Georgia Medical Association Journal, Atlanta

38:271-316 (July) 1949

Circular Thigh Amputation for Arteriosclerotic Gangrene. J. G. Durden Jr., W. G. Whitaker Jr. and R. L. Robertson.—p. 271.
Use of Anticoagulants in Surgical Practice. C. H. Richardson Jr. —p. 274.
Insulin Mixtures in Diabetes. C. W. C. Moore and C. Moore Jr. —p. 277.
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A Brighter Future for Older People. O. S. English.—p. 217.
Age-Factor in the Brain-Lesions Produced by Desoxycorticosterone Overdosage. P. S. Timiras, C. Faribault and H. Selye.—p. 225.
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Hawaii Medical Journal, Honolulu

8:397-492 (July-Aug.) 1949

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Illinois Medical Journal, Chicago

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Journal of Allergy, St. Louis

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Ability of Soil Microorganisms to Decompose Steroids. A. Schatz, K. Savard and I. J. Pintner.—p. 117.
Simplified Liquid Culture Medium for Growth of Hemophilus Pertussis. W. F. Verwey, E. H. Thiele, D. N. Sage and L. F. Schuchardt.—p. 127.
Electron Microscopy of Heated Bacteria. C.-G. Hedén and R. W. G. Wyckoff.—p. 153.
Survivor Curves of Bacteria Exposed to Surface-Active Agents. H. Migaki and E. C. McCulloch.—p. 161.
Relationship Between Growth and Mutation in Pseudomonas Fluorescens. E. Engelsberg and R. Y. Stanier.—p. 171.
Consequences of Mutation During Growth of Biochemical Mutants of Escherichia Coli. F. J. Ryan and L. K. Schneider.—p. 181.
Growth Inhibition of Tubercle Bacilli by Analogues of Phenylalanine. H. Pope.—p. 223.
*In Vivo Activity of Neomycin. S. A. Waksman, J. Frankel and O. Graessle.—p. 229.
Method for Determination of Rate of Growth of Tubercle Bacilli by Use of Small Inocula. G. P. Youmans and A. S. Youmans.—p. 247.
Streptomycin-Dependent Tubercle Bacilli: Simple Method for Isolation. D. Yegian, V. Budd and R. J. Vandevelinde.—p. 257.
Strain Differences in Oral Lactobacilli and Relation to Dental Caries. W. E. Clapper and M. E. Heatherman.—p. 261.

Neomycin.—Neomycin is produced by a member of the genus Streptomyces, which has yielded such compounds as streptothricin, streptomycin, chloramphenicol and aureomycin. Waksman and his associates state that crude preparations of neomycin in concentrations of 2,000 to 5,000 units were well tolerated, when injected subcutaneously into mice weighing 15 to 20 Gm. These concentrations are at least 20 to 50 times the protective concentration of this antibiotic. Neomycin did not exert any serious toxic effects when instilled into the rabbit's eye. Neomycin was more effective than streptomycin in suppressing infection of mice with Staphylococcus aureus. It was as effective on the streptomycin-resistant strains of this organism as on the sensitive strains. Neomycin in oral administration was more effective than streptomycin in protecting mice infected intraperitoneally with Staph. aureus. Neomycin was more effective than streptomycin in suppressing infections caused in mice and in chick embryos by Salmonella schottmülleri. Neomycin proved to be highly effective, far more than streptomycin, against Eberthella typhosa in mice. The reported investigations were conducted with rather crude preparations of neomycin. Judged by analogy to other antibiotics produced by members of the genus Streptomyces, notably streptothricin and streptomycin, these preparations can be considered as not more than 10 to 20 per cent pure. What effect the removal of impurities will have on the activity of this antibiotic is difficult to foretell. Purification should not reduce the potency of neomycin but may reduce its toxicity.

Journal of Clin. Endocrinology, Springfield, Ill.

9:579-690 (July) 1949

Estrogen Production by Testis. M. Berthrong, W. E. Goodwin and W. W. Scott.—p. 579.
Metabolic Actions and Fate of Intravenously Administered Adrenocorticotropic Hormone in Man. G. Sayers, T. W. Burns, F. H. Tyler and others.—p. 593.
Renal Clearance of Chorionic Gonadotropic Hormone in Pregnancy, in Neoplasm of Testis and Hydatidiform Mole. C. F. Gastineau, A. Albert and L. M. Randall.—p. 615.
Coarctation of Aorta Associated with Abnormal Digits, Ovarian Insufficiency and Shortness of Stature. M. L. Goldman, H. A. Schroeder and P. H. Futcher.—p. 622.
Ovarian Granulosa Cell Tumor and Acromegaly. H. Speert.—p. 630.
Estimation of Urinary Gonadotropin of Nonpregnant Human by Mouse Uterine Weight and Ovarian Hyperemia Responses. C. W. Lloyd, M. Morley, K. Morrow and others.—p. 636.
Excretion of Neutral Lipid-Soluble Reducing Substances by Infants. C. F. Matson and B. B. Longwell.—p. 646.

9:691-794 (Aug.) 1949

Use of Potassium in Therapy. J. E. Howard and R. A. Carey.—p. 691.
Changes in Circulating Eosinophils in Women During Menstrual Cycle and Reproduction. M. E. Davis and B. E. Hulit.—p. 714.
Use of Human Vaginal Smear in Assay of Estrogens. W. E. Brown and J. T. Bradbury.—p. 725.
Progesterone: Comparison of Intramuscular, Oral and Sublingual Routes of Administration. W. Bickers.—p. 736.
Effect of Alpha-Tocopherol Administration on Pregnanediol Excretion. G. E. S. Jones, E. Delfs and H. M. Stran.—p. 743.
Transport and Excretion of Uric Acid in Man: V. Sex Difference in Urate Metabolism with Note on Clinical and Laboratory Findings in Gouty Women. W. Q. Wolfson, H. D. Hunt, R. Levine and others.—p. 749.
Constancy of Serum Precipitable or Protein-Bound Iodine in Healthy Adults. T. S. Danowski, S. Hedenburg and J. H. Greenman.—p. 768.
Masculinizing Tumor of Ovary in Postmenopausal Woman. H. J. Winsauer and J. C. Manning Jr.—p. 774.
Pheochromocytoma with Hypothalamic Manifestations and Excessive Hyper-Metabolism: Case Report. W. Rabb and R. H. Smithwick.—p. 782.

Journal of Experimental Medicine, New York

90:97-180 (Aug.) 1949

Canine Hemophilia: Observations on Course, Clotting Anomaly and Effect of Blood Transfusion. J. B. Graham, J. A. Duckwalter, L. J. Hartley and K. M. Brinkhous.—p. 97.
Isolation from Cases of Infantile Diarrhea of Filtrable Agent Causing Diarrhea in Calves. J. S. Light and H. L. Hodes.—p. 113.
*Influence of Diet on Iron Absorption: I. Pathology of Iron Excess. T. D. Kinney, D. M. Hegsted and C. A. Finch.—p. 137.
*Id.: II. Interrelation of Iron and Phosphorus. D. M. Hegsted, C. A. Finch and T. D. Kinney.—p. 147.
Nucleic Acids and Production of Antibody by Plasma Cells. W. E. Ehrich, D. L. Drabkin and C. Forman.—p. 157.
Histochemical Changes in Lymphocytes During Production of Antibodies in Lymph Nodes of Rabbits. T. N. Harris and S. Harris.—p. 169.

Diet and Absorption of Iron.—According to Kinney and associates excessive deposition of iron in tissues depends on either excessive absorption or redistribution of iron within the body, since there is little excretion of iron in animals or man. The authors discuss the excessive absorption of iron. They point out that in hemochromatosis of South African natives on deficient diets, large deposits of iron are found in the parenchymal tissue of the liver and in other organs. Experimental work on the effect of diet on absorption of iron so far has been directed toward iron deficiency. Their studies show that iron absorption is excessive in animals receiving certain diets. Rats placed on a corn grit diet and added iron absorbed large amounts of iron in contrast to control groups. The histologic picture was that of progressive hemosiderosis of the hepatic parenchyma and of the reticuloendothelial system. On chemical analysis, the iron content of the liver was found to be greatly increased. This supports the concept that the liver represents the chief storage organ for iron so absorbed.

Interrelation of Iron and Phosphorus in Diet.—From studies of the dietary factors primarily involved in the failure of animals fed the corn grit and lard diet to control iron absorption, it appeared to Hegsted, Finch and Kinney that the low phosphorus content of the iron-supplemented corn grit diet is the primary cause of the abnormally high absorption of iron.

Iron absorption can be reduced by the addition of phosphate salts to this diet. The absolute amount of iron and/or phosphorus in the diet as well as the iron-phosphorus ratio influences the amount of iron absorbed.

Journal of Lab. and Clinical Medicine, St. Louis

34:1029-1174 (Aug.) 1949

*Effect of Rigid Sodium Restriction in Patients with Cirrhosis of the Liver and Ascites. W. J. Eisenmenger, E. H. Ahrens Jr., S. H. Blondheim and H. G. Kunkel.—p. 1029.
Hyperbilirubinemic Effect of Sodium Nicotinate. M. Stefanini.—p. 1039.
Cholesterol-Desoxycholic Acid: Stable Antigen for Use in Flocculation Test for Liver Dysfunction. I. Comparison with Hanger Cephalin-Cholesterol Test. A. Steinberg.—p. 1049.
Cryoglobulin Present in High Concentration in Plasma of Case of Multiple Myeloma. R. M. Hill, S. G. Dunlop and R. M. Mulligan.—p. 1057.
Immunochemical Estimation of Rate of Disappearance of Transfused Gamma Globulin from Blood in Two Cases of Hypoproteinemia. A. Bendich and E. A. Kabat.—p. 1066.
*Sensitizations to the Factor Rh in Negroes. R. K. Waller and M. Waller.—p. 1071.
Nebulized Pyribenzamine in Nasal and Bronchial Allergy. S. M. Feinberg and T. B. Bernstein.—p. 1078.
Adaptability of Mice to Laboratory Diagnosis of Tuberculosis. R. A. Patnode, M. M. Cummings and G. A. Spendlove.—p. 1081.
Serologic Relationship of Fungus Antigens. S. B. Salvin.—p. 1096.
Electrocardiogram of Normal and Malaria-Infected Monkeys. A. Ruskin and R. H. Rigdon.—p. 1105.
Lethal Effects and Electrocardiographic Changes Produced by Quinine Dihydrochloride in Malaria-Infected Monkeys. R. H. Rigdon and A. Ruskin.—p. 1109.
New Intramuscular Preparation of Quinidine (Quinidine Gluconate). S. Bellet and J. Urbach.—p. 1118.
Study of Complete Parenteral Alimentation in Dogs. H. C. Meng and F. Early.—p. 1121.
Nutritive Value of Intravenously Administered Hydrolyzed Human Serum Albumin in Man. R. D. Eckhardt and C. S. Davidson.—p. 1133.
Absorption of Unemulsified and Emulsified Vitamin A in Sprue. H. J. Fox.—p. 1140.

Sodium Restriction in Cirrhosis of the Liver and Ascites.—Eisenmenger and co-workers treated 13 patients with cirrhosis of the liver and long-standing ascites by rigid sodium chloride limitation in the diet. All but 1 of the 13 patients were able to tolerate the low sodium regimen for at least three months without ill effects. Ascites formation ceased for three months in these 12 patients. Urine output increased in each case commensurate with decreased fluid retention. In 4 patients ascites did not form again when a normal sodium chloride intake was tried after three months; ascites did recur in 8 patients. All the patients had a rise in serum proteins on the low sodium diet. This is explained primarily on the basis of retention in the serum of protein which previously had been lost in the ascitic fluid. A high protein and high caloric diet could be maintained despite rigid salt limitation by use of newly available low sodium protein supplements. In all the patients the diet appeared to be beneficial in stopping the malignant course brought about by removal of protein through paracenteses after depletion, thus enabling dietary treatment to become effective. The long term clinical results are difficult to evaluate, but the fact that ascites formation could be completely controlled by rigid sodium restriction was clearly evident.

Rh Sensitization in Negroes.—The Wallers examined 3,115 consecutive obstetric clinic patients, 2,696 Negroes and 419 Caucasians, for blood groups, Rh factor and presence of isoantibodies. One hundred and ninety-seven Negroes and 73 Caucasians were observed to be Rh negative. Among the 197 Rh-negative Negroes, 8 were found to be sensitized to Rh, and among the 73 Caucasians 3 were shown to have Rh antibodies. Sensitization was present in 4.06 per cent of the Negroes and 4.1 per cent of the Caucasians. Three-tenths per cent of the total Negro population and 0.7 per cent of the total Caucasian population had Rh antibodies. The ratio of Negro to white Rh-negative persons in this series is 1:2.4, and the corresponding ratio of sensitized patients, 1:2.7. Presumptive evidence is submitted that Rh-negative Negroes are sensitized at the same rate as Caucasians. The total number of sensitized patients is shown to be directly proportional to the frequency of Rh-negative reactions in a given population. The incidence of affected Negro children in the authors' series was about 1:900 pregnancies. The reasons for the failure to find the expected number of cases of erythroblastosis in Negro infants are numerous. Not all immunized mothers will have sufficiently potent antibodies to produce clinical symptoms in their offspring. A certain proportion will have Rh-negative unaffected children. The pigmented skin makes the diagnosis of icterus and anemia difficult. Negro multiparas usually stay in the hospital for only twenty-four to forty-eight hours after delivery, which removes their offspring from clinical observation during the time symptoms may develop. Because pronounced jaundice was unusual in the authors' group and severe anemia rather common, the condition in many cases may have been diagnosed in the past as anemia of the newborn.

Journal of Thoracic Surgery, St. Louis

18:435-590 (Aug.) 1949. **Partial Index**

*Clinical Experiences with Application of Polythene Cellophane upon Aneurysms of Thoracic Vessels. O. A. Abbott.—p. 435.
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Contralateral Spontaneous Pneumothorax Following Lobectomy. G. E. Gleason and E. M. Kent.—p. 473.
Primary Chondrosarcoma of the Lung. L. M. Lowell and J. E. Tuhy.—p. 476.
Lobectomy in Coccidioidomycosis: Report of Two Cases. J. A. Moore, J. D. Murphy and D. E. Ward Jr.—p. 484.
Carcinoma of the Esophagus: Use of Rigid Indwelling Esophageal Tube. A. L. Brown.—p. 493.
Decollation of Intrapleural Adhesions by Open Extrapleural Pneumonolysis. B. C. Thompson.—p. 496.
Mediastinal Tumors of Blood Vascular Origin. W. D. Seybold, J. R. McDonald, O. T. Clagett and S. W. Harrington.—p. 503.
Use and Abuse of Bronchoscopy in Allergic Asthma. G. L. Waldbott.—p. 526.
Experimental Observations on Embolism of Pulmonary Lobar Arteries. M. Hara and J. R. Smith.—p. 536.
Relative Effectiveness of Parenteral, Intratracheal and Aerosol Penicillin in Chronic Suppurative Disease of the Lung. E. A. Gaensler, J. F. Beakey and M. S. Segal.—p. 546.
Lipoid Granuloma of the Lung Following Bronchography with Iodized Oil. R. P. Storrs, J. R. McDonald and C. A. Good.—p. 561.
*Effect of Pneumonectomy on Pulmonary Function. W. E. Burnett, J. H. Long, C. Norris and others.—p. 569.
Lactation Following Thoracoplasty and Pneumonectomy. D. Salkin and E. W. Davis.—p. 580.

Polythene Cellophane in the Treatment of Thoracic Vessels.—Abbott treated 32 patients by applying sterilized polythene cellophane about the aneurysm of a thoracic vessel, utilizing internal wiring as well in 4 instances. The method aims to produce a periarterial fibroblastic reaction in the hope of ultimate obliteration of the aneurysmal cavity or of at least sufficient strengthening of the wall to prevent its rupture. The majority of the aneurysms were syphilitic in origin. There were aneurysms of congenital origin, arteriosclerotic and dissecting types. There was 1 instance of a diffuse aneurysmal dilatation of the pulmonary artery of congenital origin, probably secondary to a massive interatrial septal defect. There was also a most unusual congenital anomaly of the descending portion of the thoracic aorta. This lesion could not be completely surrounded by the cellophane so that definite benefit from this type of surgical intervention was not obtained. One would have to consider here the possibility of a resection of this portion of the aorta and some method of reconstruction. One aneurysm of the main pulmonary artery was treated which was observed to be in association with diffuse sclerosis of the pulmonary and systemic arteries in a young woman. It is doubtful whether this procedure would have benefited the patient had a successful postoperative course occurred. When an irritative substance is placed within the pericardium, an inner layer of the non-irritative cellophane should be utilized. This procedure has been applied in 2 instances in the presence of active massive hemoptysis. In 1 of these cases it was used as an aid in the closure of a fistula between the aneurysm and the lung. The danger of separating an area of aneurysmal disease from a point of bony contact is reemphasized. Major tracheal or bronchial obstruction, secondary to an aneurysm, must be corrected by a preliminary decompression operation before any open intrathoracic operative procedures. A sufficient amount of benefit has been derived from the application of polythene cellophane in these patients with far-advanced obstruction to consider continued use of the method. The combination of the indirect methods of correction of aneurysmal disease by application of cellophane externally and by internal wiring probably presents certain advantages not inherent in any one method of indirect approach.

Pneumonectomy and Pulmonary Function.—Burnett and co-workers studied pulmonary function by external spirometry and bronchial spirometry, before and after pneumonectomy, in 24 patients, 17 men and 7 women between the ages of 35 and 66 years. Pneumonectomy was performed in 21 instances for pulmonary neoplasm and in the remaining 3 for extensive unilateral bronchiectasis. Pneumonectomy produced little or no change in the over-all resting tidal volume, minute volume and oxygen consumption. Pneumonectomy usually reduced the maximum breathing capacity and the breathing reserve by reducing the depth of respiration during maximal respiratory effort. This lack of change in over-all resting pulmonary function after pneumonectomy was due to compensatory adjustments of the remaining lung, namely (*a*) an increase in tidal volume, (*b*) an increase in minute volume and (*c*) an increase in the oxygen uptake. There was little or no increase in the depth of respiration of the remaining lung during maximum respiratory effect. What increase occurred in the maximum breathing capacity of the remaining lung was due to an increase in the rate of respiration. There was a lessened ability in most patients to increase the ventilation of the lungs on demand after the operation. This decrease in breathing reserve was associated with subjective dyspnea only if the patient was required to undertake some activity requiring considerable muscular effort. Most of the patients undergoing pneumonectomy were in the older age group, so their normal activities were seldom strenuous enough to cause this. The patients who showed considerable functional impairment after pneumonectomy usually had other factors complicating the postoperative course such as hemiplegia or spreading carcinoma.

Journal of Urology, Baltimore

62:93-266 (Aug.) 1949. **Partial Index**

*Benign and Malignant Pheochromocytomas with Necropsies: Benign Case with Multple Neurofibromatosis and Cavernous Hemangioma of Fourth Ventricle; Malignant Case with Widespread Metastases and Bronchiogenic Carcinoma. F. B. Mandeville and P. F. Sahyoun.—p. 93.
*Pancreatic Cysts Simulating Renal Disease. E. P. Stone.—p. 104.
Renal Colic in Cases of Tumor and Tuberculosis of Kidney: Roentgenologic Views. O. Olsson.—p. 118.
Value of Nephrectomy in Treatment of Bilateral Renal Tuberculosis: Report of Clinical and Experimental Data. M. E. Greenberger and A. Sporer.—p. 128.
Preliminary Nephrostomy Preparatory to Secondary Nephrectomy. C. E. Haines Jr. and F. K. Garvey.—p. 133.
Squamous Cell Carcinoma of Renal Pelvis: 3 Case Reports and Review of Literature. H. Q. Gahagan and W. K. Reed.—p. 139.
Retrocaval Ureter: Report of Case with Successful Plastic Repair. T. P. Shearer.—p. 152.
Cutaneous Metastasis of Bladder Carcinoma. L. E. McCrea.—p. 158.
Hemoglobinemia and Hemoglobinuric Nephrosis Complicating Transurethral Resection of Prostate. L. M. Woodruff and H. I. Firminger. —p. 168.
Survival in Cancer of Prostate. T. E. Canning, C. M. Norfleet Jr. and F. K. Garvey.—p. 185.
Problems of Reconstruction in Urology. F. M. Jacobs.—p. 196.
Hydrocalycosis. O. J. Wilhelmi.—p. 206.
Ureteral Obstruction Associated with Carcinoma of Cervix. H. M. Spence and D. M. Hare.—p. 219.
Transurethral Resection of Large Prostates. H. A. O'Brien, J. D. Mitchell Jr. and E. C. St. Martin.—p. 225.
Intraprostatic Local Anesthesia for Transurethral Prostatic Resections. M. K. O'Heeron, A. W. Miles and M. G. Rape.—p. 231.
Pelvic Myalgia: Complication of Posterior Urethritis in Males and Females. N. B. Powell.—p. 245.
Cancer of Scrotum. C. C. Higgins and J. G. Warden.—p. 250.
Medical Treatment of Urinary Tuberculosis: Case Reports. M. Schattyn. —p. 257.

Pheochromocytoma.—Mandeville and Sahyoun report 2 cases of pheochromocytoma in adults, both of whom came to necropsy and showed several unusual features. The first case was that of a woman aged 55 with multiple neurofibromatosis (von Recklinghausen's disease), who died suddenly following severe trauma and multiple fractures. Necropsy showed a single benign adrenal pheochromocytoma. The cause of her hypertension had been unrecognized clinically over a twenty-eight year period of medical study and multiple surgical operations. A left upper quadrant abdominal mass had been felt on one physical examination seven years before her death, which occurred suddenly eight hours after an automobile accident. In the second case a man aged 63 had malignant bilateral adrenal pheochromocytomas showing multiple metastases and a left bronchogenic carcinoma with massive pleural effusion. The first case adds another report of sudden death following severe accidental trauma in a patient with clinically unexplained hypertension and proved benign pheochromocytoma to the medical literature. The association with multiple neurofibromatosis has appeared in the literature less than forty times. This patient also had a cavernous hemangioma of the fourth ventricle of the brain, which blocked incompletely the ventricular system and led to cerebral exploration. This has not been reported previously in a case of pheochromocytoma, although von Recklinghausen's disease in many instances shows anomalies in the development of the central nervous system. The malignant pheochromocytoma was believed to be primary in the retroperitoneal region on the left side with involvement of both adrenals, tail of the pancreas, liver, capsule of the spleen, peritoneum, diaphragm and parietal pleura. The malignant pheochromocytoma was associated with another neoplastic process in the left lung, a bronchogenic carcinoma. Both were believed to contribute to the development of a massive hemorrhagic pleural effusion. There is on record the association of a pheochromocytoma with a carcinoma of the thyroid, but not with a bronchogenic carcinoma. There are few cases in the literature in which pheochromocytoma developed widespread metastases as in this patient with malignant pheochromocytoma. It is interesting that the dissemination in this case appeared to be by continuity and along the lymphatic system.

Pancreatic Cysts Simulating Renal Disease.—Stone reports vague epigastric pain, heartburn, nausea and vomiting of some months' duration in a man who had attributed them to alcoholic excesses. Examination revealed tenderness in the left costovertebral angle, and an oval, firm, nonmovable tender mass in the left upper quadrant of the abdomen. Gastrointestinal studies and pyelograms led to the diagnosis of a cyst of the pancreas. At operation the lower pole of the left kidney appeared to be continuous with a large mass which extended up to the diaphragm. There was no line of demarcation between the renal substance and the mass, which, when freed from adhesions, felt firm and solid. It was now believed that the mass was a renal tumor. Eventually the kidney, a thick capsule and a cyst were removed. The patient died three hours after the operation. It was not appreciated that although most pancreatic cysts are thin walled some may be thick walled. Had the possibility of such a thick-walled cyst been realized, aspiration would have revealed the correctness of the preoperative diagnosis, and drainage or marsupialization could have been performed with little risk to the patient. The author found 9 similar cases in the literature, with a correct diagnosis in only 2. The following studies may be helpful in the diagnosis of a pancreatic cyst: gastrointestinal roentgenography, blood amylase determinations and analysis of the past history for prior episodes of biliary attacks, acute pancreatitis or abdominal trauma. Resection effects a cure, but this is technically impossible in many instances. Marsupialization, with or without partial resection, effects a cure in a large proportion of cases. A pancreatic cyst may have a thick, gristly false capsule which deceives the surgeon into believing that he is dealing with a solid tumor. Attempted aspiration can do no harm.

Maine Medical Association Journal, Portland

40:173-202 (July) 1949

Juvenile Deliquency and Criminal Homicide. D. A. Thom.—p. 176.
Industrial Medicine at Saco-Lowell Shops. F. W. Barden.—p. 181.

40:203-250 (Aug.) 1949

Malignant Disease of the Larynx. G. O. Cummings.—p. 204.
Toward Better Prenatal Care. R. V. Lorimer.—p. 208.
Acute Appendicitis with Perforation: Review of 33 Cases. R. L. Taylor. —p. 213.
Epidemic Diarrhea of the Newborn. J. E. Porter, C. A. Stetson and T. A. Foster.—p. 217.
Twenty Years' Experience with Cancer of Cervix. W. Holt.—p. 221.
Anesthesia for Cardiac Patient. J. R. Lincoln and R. Martin.—p. 226.
Intestinal Obstruction Due to Enterocholelithiasis. J. F. Appel.—p. 229.
State Aid—Enigma of Hospital Administration. J. C. Barker.—p. 233.
Why—Medical Records? B. K. Moody.—p. 235.
Medical Social Service at the Maine General Hospital. E. W. Klassen. —p. 239.
The Problem of the Unmarried Mother. R. M. Dalton.—p. 241.
Hospital Diets and Doctors. E. Grimmer.—p. 243.

Minnesota Medicine, St. Paul

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Minnesota Centennial—Its Medical History. E. M. Hammes.—p. 797.
Endometriosis. C. J. Ehrenberg.—p. 805.
Pathologic Aspects of Endometriosis. M. B. Dockerty.—p. 806.
Tumors of Optic Disc: Report of Case. E. R. Bray.—p. 809.
Impressions from European Neurosurgical Clinics. L. A. Titrud.—p. 811.
Delayed Primary Closure of Wounds. F. S. Babb.—p. 815.
Differential Diagnosis in Pulmonary Shadows Observed on X-Ray Films. H. Mark.—p. 816.

New England Journal of Medicine, Boston

241:253-286 (Aug. 18) 1949

*Roseola Infantum (Exanthem Subitum). W. Berenberg, S. Wright and C. A. Janeway.—p. 253.
Major Urologic Considerations in Paraplegia. H. S. Talbot, M. K. Lyons and A. J. Bassell.—p. 259.
*Mumps Complicated by Preceding Myelitis: Report of Fatal Case. A. C. Silverman.—p. 262.
Medical Treatment of Acute Pulmonary Abscess. W. J. Walker.—p. 266.
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Abscess of Lung.—p. 277.
Lactating Fibroadenoma of Breast.—p. 280.

Roseola Infantum.—According to Berenberg and co-workers, roseola infantum (exanthem subitum) is a relatively asymptomatic febrile disease, with a paucity of physical observations, of three to five days' duration and followed by a morbilliform eruption. The appearance of the rose pink rash, occurring predominantly on the neck and trunk, ordinarily coincides with the subsidence of fever. It is the commonest exanthem of infancy. The disease may be an almost universal infection under 5 years. It is most prevalent in spring and autumn. There is no difference in incidence between the sexes. Ninety-five per cent of the cases occur between the ages of 6 months and 3 years. Incubation periods of ten and fifteen days seem to be most likely, but on 3 occasions the disease appeared thirty to ninety days after a known intimate exposure. The possibilities of a large carrier population and a modified form of the disease are to be considered. Evidence favors a virus etiologic agent. The prognosis is for the most part excellent, but more serious unrecognized and occasionally fatal variants of the usual clinical picture should be kept in mind. Complications include convulsions, encephalitis and infrequently hemiplegia. The disease can be differentiated from the other common exanthems. The treatment is symptomatic.

Myelitis and Mumps.—Silverman reports a fatal case of mumps myelitis in a physician aged 37. There had recently been a number of cases of mumps in the patient's area, and he had seen 2 cases with meningoencephalitis. Symptoms and signs of myelitis preceded parotid swelling by three days. Death ensued within eight days and was caused by pulmonary involvement consistent with virus disease, but whether it was caused by the primary virus is problematic. Necropsy revealed focal lymphocytic infiltration of the parotid gland with preservation of the general acinar cell structure and pyknosis of some nuclei. Sections from the cerebral cortex revealed some demyelinization and lymphocytic infiltration. Sections from the anterior horns of the cervical cord showed appreciable perineuronal edema. Both lungs were heavier than normal, deep purple and nonaerated. Sections from the lungs showed polymorphonuclear exudate within the bronchial lumen, sloughing of bronchial epithelium and infiltration of the submucosa. The alveoli were relatively free of exudate, although scattered lymphocytes, mononuclear cells and plasma cells were seen. The interstitial tissue also showed a mild infiltration by these cells. In the literature on mumps there is no description of the disease in the lung as in the author's case. The virus studies supplied only negative results, but failure to isolate mumps virus from the postmortem tissues can have no bearing on the pathologic diagnosis. The new complement-fixation antigens, the virus-bound (V) antigen and the soluble (S) antigen were not as yet available. Since then the use of both these antigens has made possible the early diagnosis of manifestations of mumps as meningoencephalitis in the absence of parotitis.

New York State Journal of Medicine, New York

49:1743-1870 (Aug. 1) 1949

Ulcerative Colitis Problem. A. F. R. Andresen.—p. 1783.
Treatment of Papillary Adenomas of Rectum. G. E. Binkley, D. A. Sunderland and C. J. Miller.—p. 1791.
Relation of Amebic Dysentery to Chronic Ulcerative Colitis. W. H. Bernhoft.—p. 1795.
Recent Advances in Antibiotic Therapy. S. Strax and L. T. Wright. p. 1797.
Colonic Dysfunction. S. M. Jordan.—p. 1802.
Ileojejunitis. B. B. Crohn.—p. 1808.
Migraine Headache Treated Successfully by Head-Traction Manipulation and Thiamin Chloride M. M. Braaf.—p. 1812.
Treatment of Paralysis Agitans with Thephorin. F. M. Berger.—p. 1817.
Review of Colon Surgery Including Rectum for Years 1947-1948 at Binghamton City Hospital. F. D. Conole and R. J. Phalen.—p. 1821.
Hesperidin-C and Capillary Fragility. W. C. Loughlin.—p. 1823.
Experience with Barton Forceps in Small Urban Hospital. L. G. Barton Jr.—p. 1825.
Clinical Evaluation of Ethinyl Estradiol in Menopause. H. Dubrow, C. S. Poole and R. I. Walter.—p. 1828.
Use of Intermittent Ambulatory Schedule of Penicillin in Oil and Wax in Treatment of Early Latent Syphilis and Syphilis in Pregnancy. G. E. Peabody and B. Webster.—p. 1829.
Migraine Problem. A. P. Friedman.—p. 1831 .

49:1871-1982 (Aug. 15) 1949

*Anorectogenital Lymphogranuloma Venereum and Granuloma Inguinale Treated with Aureomycin. A. Prigot, L. T. Wright, M. A. Logan and F. R. deLuca.—p. 1911.
Gastroenteritis in Man Due to Filtrable Agent. I. Gordon, H. S. Ingraham, R. F. Korns and R. E. Trussell.—p. 1918.
Rehabilitation of Arm Amputee. H. H. Kessler.—p. 1921.
Basis of Treatment in Postphlebitic Syndrome. S. T. Glasser.—p. 1923.
Old Age. T. G. Klumpp.—p. 1929.
Uses and Abuses of Physical Therapy in Industrial Medicine and Surgery. R. Kovacs.—p. 1934.
Fungous Infections of Skin and Scalp: New Approach to Their Treatment. F. Reiss and D. D. Doherty.—p. 1939.
Discussion of Cancer Prevention and Detection Centers. L. B. Goldman —p. 1944.
Varicose Veins: Different Concept and Approach to Their Treatment. R. V. Schatken.—p. 1947.
Complete Versus Supravaginal Hysterectomy. H. S. Irons.—p. 1951.
Hematologic Disorders. E. G. Allen.—p. 1956.
Hay Fever as Public Health Problem. L. C. Lazarowitz.—p. 1960.

Aureomycin in Anorectogenital Lymphogranuloma Venereum.—Prigot and associates report 49 cases of lymphogranuloma venereum and 13 cases of granuloma inguinale treated with aureomycin at their hospital. In their experience over the past twenty-four years with several hundred of these cases, they have never observed such eminently satisfactory results in so short a period. This paper confirms their previous observations and is a report on 14 additional cases of lymphogranuloma venereum and 1 of granuloma inguinale, the latter especially chosen because of its unusual rectal manifestations. It also includes a follow-up report on 12 of 35 originally reported cases of lymphogranuloma venereum and 10 of 12 cases of granuloma inguinale, all of which were treated with aureomycin. The drug was administered by the oral, intravenous and intramuscular routes. Effective blood levels were obtained if proper dosage was used regardless of the route. Aureomycin is the treatment of choice for granuloma inguinale and for the strains of lymphogranuloma venereum with which the authors had to deal.

North Carolina Medical Journal, Winston-Salem

10:293-336 (June) 1949

Reflections, Protestations, and Suggestions of Member of Loyal Opposition. H. J. Morgan.—p. 293.
Sun and the Skin. J. M. Hitch.—p. 299.
Nutrition Surveys. H. R. Sandstead and E. S. Osborne Jr.—p. 304.
Etiology and Nonsurgical Treatment of Cataract. E. M. Blake.—p. 309.
Osteogenic Sarcoma. C. A. Zarzecki.—p. 312.
Further Studies on Use of Rectal Sodium Pentothal in Obstetrics. E. W. Furgurson.—p. 314.
Dorothea Lynde Dix: America's Greatest Woman. F. R. Taylor.—p. 317.
Surgical Treatment of Massive Hemorrhage from Peptic Ulcer. J. W. Davis.—p. 320.
Incarceration of Meckel's Diverticulum in Inguinal Hernia: Report of Case and Review of Literature. F. M. S. Patterson.—p. 322.

Physiological Reviews, Baltimore

29:195-280 (July) 1949

Metabolism of Parasitic Helminths. E. Bueding.—p. 195.
Determination of Amino Acids by Microbiological Assay. M. S. Dunn. —p. 219.
Exophthalmos. C. Brunton.—p. 260.

Proc. of Staff Meet. of Mayo Clinic, Rochester, Minn.

24:405-428 (Aug. 3) 1949. **Partial Index**

Effect of Arteriovenous Fistula on Growth of Bone: Preliminary Report. J. M. Janes and J. E. Musgrove.—p. 405.
*Intrathyroid Hyperfunctioning Parathyroid Adenomas: Report of 2 Cases. B. M. Black and A. L. Haynes.—p. 408.

Parathyroid Adenomas Within the Thyroid.—Black and Haynes say that intrathyroid parathyroid adenomas have been considered exceedingly rare. The finding of 2 among less than 100 cases of parathyroid adenomas along with 9 previously reported cases among a collected series of 281 cases suggests that this location is the site of adenomas with sufficient frequency to be of some significance in the surgical problem of hyperparathyroidism.

Public Health Reports, Washington, D. C.

64:961-990 (Aug. 5) 1949

What is a Reportable Case of Tuberculosis? C. Northrop, R. J. Anderson and H. I. Sauer.—p. 961.
Simple Apparatus for Controlling Temperatures of Film-Processing Solutions. W. W. Van Allen.—p. 968.
Effective Nursing Care for the Tuberculous. C. Bush, E. H. McNett, L. Petry and M. B. Naylor.—p. 971.
Characteristics of Commercial X-Ray Screens and Films—VIII. W. W. Van Allen.—p. 979.

64:991-1020 (Aug. 12) 1949

Hospital Survey and Construction Program: Progress Report. V. M. Hoge.—p. 991.

64:1021-1060 (Aug. 19) 1949

Epidemiologic Study of Brucellosis in Minnesota. R. L. Magoffin, P. Kabler, W. W. Spink and D. Fleming.—p. 1021.
Relation of Human and Bovine Brucellosis in Minnesota. D. S. Fleming and M. H. Roepke.—p. 1044.

Rhode Island Medical Journal, Providence

32:361-416 (July) 1949

Recent Trends in Surgery of the Thorax. J. M. Beardsley.—p. 375.
Ruptured Intervertebral Discs—Diagnosis and Treatment. L. A. Senseman, H. Hamlin and H. Umstead.—p. 378.
Unusual Complication of Ureterolithotomy. H. M. Kechijian.—p. 381.
Dietary Factors in Cardiovascular Diseases. S. Proger.—p. 382.
National Health Plans—British and American. R. E. S. Young.—p. 388.

Surgery, St. Louis

26:161-330 (Aug.) 1949

*Acute Pancreatitis: Pathways of Enzymes into Blood Stream. J. M. Howard, A. K. Smith and J. J. Peters.—p. 161.
Cleft Left Upper Lobes and Split Anterior Bronchus. E. A. Boyden.—p. 167.
Experimental Tendon Repair Within Flexor Tunnels: Use of Polyethylene Tubes for Improvement of Functional Results in Dog. R. I. Gonzalez.—p. 181.
Hemipelvectomy. M. M. Ravitch.—p. 199.
Sulfamethazine in Treatment of Urinary Infections Due to Gram-Negative Bacilli. A. M. Rutenburg and F. B. Schweinburg.—p. 215.
Meconium Peritonitis. J. R. Low, G. Cooper Jr. and L. Cosby Jr.—p. 223.
*Clinical Experiences with Artificial Kidney. C. B. Ripstein, J. T. MacLean, N. K. M. DeLeeuw and G. G. Miller.—p. 229.

Acute Pancreatitis: Pathways of Enzymes into Blood Stream.—Howard and his associates feel that one of the problems of the pathologic physiology of acute pancreatitis is to explain the rise in serum enzymes which accompanies it and to determine whether this elevation has significant clinical effects. This study has been undertaken to show directly whether or not the injured pancreas is the source of the additional serum amylase and, if so, by what route the additional enzyme reaches the serum. Ten dogs were used for the experiments. The dog was chosen because his salivary glands do not secrete amylase; therefore, one variable was eliminated. The experiment was designed to produce two somewhat comparable episodes of acute pancreatitis in each dog within two weeks. In the first experiment the pancreatitis was produced by ligation and dissection of the pancreatic ducts. This assured complete absence of pancreatic enzymes from the gastrointestinal tract in secondarily induced pancreatitis. Ligation of the thoracic duct, after the first experiment was completed, excluded the duct from transporting enzymes at the time of the second experiment. This second pancreatic trauma was produced by injection of bile into the pancreatic ducts of a dog in which the pancreatic enzymes thus had access to the body only through the blood stream. The concentration of amylase in the serum rose rapidly even though the pancreatic and thoracic ducts were obstructed. The concentration of serum amylase increased approximately 100 per cent in the femoral vessels within the first hour following the production of a bile-induced pancreatitis. At the same time the concentration of amylase in the serum of the pancreatic veins increased approximately 500 per cent. An intermediate concentration was found in the portal vein. Comparison of the concentration of amylase in the aortic blood serum and in blood serum from the veins of the damaged pancreas reveals a much higher concentration in the venous blood serum. The authors conclude that the pathway of the enzyme into the blood stream is chiefly that of absorption directly into the blood stream from the damaged pancreas, an observation which substantiates the conclusion of Popper and Necheles.

Clinical Experiences with Artificial Kidney.—Ripstein and his co-workers used the Kolff artificial kidney with certain modifications. The chief value of such an apparatus is in the treatment of uremia due to reversible conditions of the kidney. A temporary clearing of the blood by dialysis may give the kidney time to recover from damage and resume function. The authors discuss the types of uremia in which dialysis is of value; the effect of dialysis on the blood chemistry, on the circulating blood and on the patient. Dialysis with the artificial kidney is well tolerated even by the poor-risk patient. The machine constitutes an arteriovenous shunt, but the capacity of the shunt is only 200 cc. a minute and this is not enough to embarrass the circulation. The rapid return of blood into the right side of the heart may theoretically cause a rise in venous pressure and lead to pulmonary congestion. The authors observed no harmful effects. In all cases the pulse rate and blood pressure remained constant throughout, and there was no evidence of cardiac failure. The authors report 6 patients in whom they employed dialysis. In 1 the method was a life-saving measure; in another good results were obtained but could hardly be attributed to the artificial kidney. A third improved following dialysis, and the other 3 died.

Tennessee State Medical Assn. Journal, Nashville

42:269-306 (Aug.) 1949

OBSTETRICAL SYMPOSIUM—TOXEMIAS OF PREGNANCY

Etiology and Early Diagnosis of Toxemias of Late Pregnancy. C. R. Green.—p. 269.
Pathology of Toxemias of Late Pregnancy. W. M. Bryan Jr.—p. 271.
Treatment of Toxemias of Late Pregnancy. H. B. Turner.—p. 273.
Goniotomy for Congenital Glaucoma. J. W. McKinney.—p. 277.
Functions of American Academy of General Practice at Crossroads in Organized Medicine. P. A. Davis.—p. 284.
Medical Aspects of Atomic Explosion. E. DeCoursey.—p. 289.

Virginia Medical Monthly, Richmond

76:381-432 (Aug.) 1949

James Thacher and his Influence on American Medicine. H. R. Viets.—p. 384.
Variable Clinical Manifestations of Sickle Cell Anemia. W. H. Higgins Jr. and E. C. Toone Jr.—p. 400.
Recogntion of Pre-Schizophrenic States. G. C. G. Thomas and D. C. Wilson.—p. 405.
Arteriosclerotic Heart Disease in Diabetics. R. L. Bailey.—p. 411.
*Analysis of 27 Reported Fatalities Immediately Following Injection of Mercurial Diuretic. T. E. Stanley.—p. 416.

Fatalities Immediately Following the Injection of Mercurial Diuretic.—Stanley collected from the literature 27 cases in which death occurred immediately after the injection of a mercurial diuretic. He makes the following suggestions: 1. The intravenous route of administration should be omitted when satisfactory diuresis can be obtained by other routes. 2. The smallest dose of a mercurial diuretic which will produce the desired response is the dose of choice. 3. The intravenous route of administration should be avoided whenever practical in persons who have previously experienced undesirable reactions following intravenous administration of a mercurial diuretic.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

57:331-396 (Aug.) 1949

Chronic and Recurrent Intestinal Obstruction. D. B. Seabrook.—p. 331.
Maternal and Fetal Mortality Study at the Huntington Memorial Hospital, 1928-1947. L. G. Baldwin.—p. 336.
Diabetes in Pregnancy. S. Z. Goodman.—p. 350.
Gynecologic Mortality Lessons. H. K. Marshall and G. Macer.—p. 365.
Giant Hypertrophic Gastritis. C. J. Berne and W. R. Gibson.—p. 388.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Journal of Cancer, London

3:161-310 (June) 1949. **Partial Index**

Malignancy of Cancer at Different Ages: Histological Study. J. C. Lees and W. W. Park.—p. 186.
Effects of Castration and Stilboestrol on Prostatic Tumours in Mice. E. S. Horning.—p. 211.
Mammary Tumours in Hybrid Mice. L. Foulds.—p. 230.
Survival of Milk Factor in Transplantable Breast Tumour in Mice. L. Dmochowski.—p. 246.
Survival of Activity of Mouse Sarcoma Tissue After Freezing and Drying. W. E. Gye, A. M. Begg, I. Mann and J. Craigie.—p. 259.
Preservation of Suspensions of Tumour Cells in Dextrose at Low Temperatures. J. Craigie.—p. 268.
Effect of Restricted Diet on Mitotic Activity in the Mouse. W. S. Bullough.—p. 275.
Attempts to Induce Epithelial Tumours in Fowls. A. Peacock and P. R. Peacock.—p. 289.
Influence of Solvents on Tissue Response to Carcinogenic Hydrocarbons. P. R. Peacock, S. Beck and W. Anderson.—p. 296.

British Journal of Industrial Medicine, London

6:125-212 (July) 1949

Care of Lead Worker. R. E. Lane.—p. 125.
*Outbreak of Cases of Raynaud's Phenomenon of Occupational Origin. J. N. Agate.—p. 144.
Skin Sensitivity to Cetrimide (CTAB). C. N. D. Cruickshank and J. R. Squire.—p. 164.
Problem of Consistent Radiological Diagnosis in Coalminers' Pneumoconiosis: Experimental Study. C. M. Fletcher and P. D. Oldham.—p. 168.
Talc Pneumoconiosis. A. I. G. McLaughlin, E. Rogers and K. C. Dunham.—p. 184.

Raynaud's Phenomenon of Occupational Origin.—Agate says that at present it is accepted that the term Raynaud's disease shall be used only for a distinct but rare symmetric vascular disorder of unknown causation, which is found mostly in young women; similarly, that Raynaud's phenomenon shall apply to a symptom or sign, namely, intermittent pallor or cyanosis of the extremities. Raynaud's phenomenon is also referred to as "dead hand," "dead fingers," "pneumatic hammer disease" and "pseudo-Raynaud's disease." He reports on the occurrence of Raynaud's phenomenon in workers who were polishing metal castings with rotary tools. A survey of 279 case histories revealed that of 234 men 163 had Raynaud's phenomenon and 71 were free from it; of 45 women 21 were affected and 24 were free from it. The attacks occurred in workers of all ages over 20 and were precipitated by cold. As a rule a worker's dominant hand was affected less often, later and less severely than the other, because of the way the tool was held. The ring and middle fingers were most affected. Cyanosis usually appears about six months after the first evidence of blanching. Younger men may be somewhat more prone to cyanosis than older men. A simple diagnostic aid in the form of cold-water immersion test is described, and its practical limitations and interpretation are discussed. Two and a half years after the first inquiry a questionnaire was circulated, and the course of the disease was estimated from the forms returned. Half of those who had been affected in the first place were of the opinion that their condition was stationary, 36 per cent claimed that there had been a deterioration in the interim; 4.9 per cent were improved. One woman claimed a spontaneous cure. In spite of slight improvement in some instances, the anatomic extent of Raynaud's phenomenon had in the main increased.

British Medical Journal, London

2:247-398 (Aug. 13) 1949

Thomas Addison: Pioneer of Endocrinology. H. Dale.—p. 347.
Principles Underlying Determination of Sex Hormones. H. de Watteville, S. Salinger and R. Borth.—p. 352.
Poliomyelitis and Social Environment. A. B. Hill and W. J. Martin.—p. 357.
Production of Dental Caries: New Hypothesis. P. Pincus.—p. 358.
Case of Psittacosis Treated with Pennicillin. J. R. Tasker.—p. 362.
Case of Monocytic Leukaemia Treated with Aminopterin. P. L. de V. Hart.—p. 363.
Isolated Unilateral Spinal Accessory Nerve Palsy of Obscure Origin: Report of 3 Cases. J. D. Spillane.—p. 365.
Case of Diaphragmatic Hernia of Congenital Origin with Perforation of Stomach. S. B. Radley and H. P. Goldsmith.—p. 366.

Journal of Tropical Medicine and Hygiene, London

52:155-176 (Aug.) 1949

Typhus Fevers in Anglo-Egyptian Sudan. E. P. Pratt, A. D. Drysdale and R. Kirk.—p. 157.
*Parasite Rate in High Altitude Malaria. J. I. Roberts.—p. 160.

High Altitude Malaria.—Roberts describes the behavior of Plasmodium falciparum at high altitudes, where the majority of infections are mild in character and the parasite rates are low. These scanty infections can be easily overlooked in blood smears, and failure to find them often leads to an intractable state of chronic debility. Frequent examinations of the blood are essential at high altitudes to eliminate any possibility of these scanty infections being present. Such infections are known to be contracted in Nairobi, the vector being Anopheles gambiae, which has a low infectivity rate in this area in spite of a plentiful food supply and a high infectivity rate among the general human population. Europeans show a greater tendency to contract these scanty infections than other races and suffer less from anemia, which may be due to greater care in adopting prophylactic measures together with a higher resistance owing to better standards of nutrition and fitness. It is generally assumed that the incidence of malaria at high altitudes is governed almost solely by the presence of Anopheles gambiae and good rainfall. When more detailed figures are studied, it is obvious that some other factor comes into play to determine the incidence and intensity of the disease. There is a decided increase in malaria rates through January to March, uninfluenced by either higher rainfall or greater density of the vector. In fact, at this particular period the rates increase even when rainfall is low and the anopheline density negligible. Then there comes the decided increase in malaria rates for ten to fourteen days prior to the onset of heavy rainfall, which will provide optimum conditions for the vector. Thus arises a suggestion that the parasite itself displays a periodicity, both in its virulence and its intensity among latent cases of malaria or in persons in whom only the scanty infections of high altitudes occur. If this were true, it would explain why prophylactic measures fail at certain periods and conversely why so often some measure, having been employed during a nonvirulent phase is hailed as a great success, only to fail at some future date.

Lancet, London

2:265-310 (Aug. 13) 1949

Twenty-Five Years of Biliary Surgery. W. Walters.—p. 265.
Simple Radiological Aid to Gasserian Injection. J. Penman.—p. 268.
*Mortality of Primary Tuberculosis in Childhood. F. J. W. Miller.—p. 274.
*Internal Mammary Lymph Chain in Carcinoma of Breast: Study of 50 Cases. R. S. Handley and A. C. Thackray.—p. 276.
Effect of Water and Salt Intake on Prickley Heat. G. O. Horne and R. H. Mole.—p. 279.
Recurring Pneumococcal Meningitis. A. P. Norman.—p. 281.
Anti-Pernicious-Anaemia Factor and White-Cell Count. J. Dedichen and P. Laland.—p. 282.
Total Serum-Fat in Hypertony. I. Harris, C. E. Vernon, N. Jacob and M. E. Roberts.—p. 283.
Human Serum Containing Anti-N Agglutinin. S. Phansomboon, E. W. Ikin and A. E. Mourant.—p. 285.

Mortality of Primary Tuberculosis in Childhood.—Miller presents figures which show the importance of tuberculosis as a cause of death in childhood. In England and Wales in 1945 one seventh of the deaths of children aged 1 to 15 years were due to tuberculosis. Tuberculosis, violence and respiratory disease were together responsible for half the deaths between the ages of 1 and 5 years. At school age tuberculosis is the chief infective cause of death in England and Wales. The mortality from tuberculosis is much higher in children of families with an adult who has infective tuberculosis than in the child population as a whole. In children up to 12 years, the younger the age of infection the greater the risk of a fatal outcome of the primary infection.

Internal Mammary Lymph Chain in Carcinoma.—Handley and Thackray point out that early cases of carcinoma of the breast, so-called stage 1 cases, show a mortality from recurrence of about 25 per cent within five years of radical mastectomy. Since stage 1 cases are those in which the carcinoma is believed not to have spread beyond the breast, this result is inexplicable unless the methods of deciding how far the

malignant process has advanced are less accurate than has been assumed. The authors show that the internal mammary lymphatic pathways are worthy of greater attention than has hitherto been paid to them and that in them lies at least part of the explanation why radical mastectomy in stage 1 carcinoma is not followed by 100 per cent cure. They made microscopic studies on the internal mammary chain in an unselected consecutive series of 50 patients with carcinoma of the breast. The internal mammary chain was invaded in 19 cases. In 16 of these the deposits were in lymphatic glandular tissue, in 2 in the connective tissues adjoining the internal mammary artery and in 1 within the lumen of a mediastinal venule. In 3 of these 19 cases the internal mammary chain alone was invaded, the axillary glands being free from growth, and in 16 both axillary and internal mammary glands were invaded. The axilla alone was invaded in 15 cases. No glandular deposits were found anywhere in 16 cases. It is remarkable that, of the 13 primary growths in the inner half of the breast which showed glandular deposits, 12 had metastasized to the internal mammary chain and only 1 had invaded the axillary lymph nodes alone. Exploration of the second intercostal space is not to be regarded as a method of treatment for carcinomatous deposits in the internal mammary chain but as a reconnaissance designed to give information about the movements of the carcinoma cells. The only method of dealing with internal mammary deposits is Sampson Handley's (1927) technic of implanting radium tubes in the medial end of the intercostal spaces, and its efficacy has not yet been unequivocally proved.

Tubercle, London

30:169-192 (Aug.) 1949

Management of Mass Radiography Suspects: Two-Year Follow-Up. J. Aspin.—p. 170.
Artificial Pneumothorax in Elderly Subjects. E. H. W. Deane.—p. 178.
Weight Changes and Sex Incidence of Tuberculosis. B. Benjamin, A. C. Dalzell and F. A. Nash.—p. 179.

Acta Medica Scandinavica, Stockholm

133:299-374 (June 14) 1949. **Partial Index**

Experiences with Tetraethylammoniumbromide. G. Biörck and B. Ejrup.—p. 299.
*Red Blood Cell Diameter in Acute Hepatitis. G. Lindgren.—p. 321.
*Decrease of Renninogenuria in Pernicious Anemia and Its Diagnostic Value in Liver-Treated Patients. O. Sylvest.—p. 346.
Studies on Pathogenesis of Rheumatic Fever: II. Antistreptolysin Titer in Acute Tonsillitis. S. Winblad, H. Malmros and O. Wilander.—p. 358.

Red Cell Diameter in Acute Hepatitis.—According to Lindgren the mean red cell diameter is frequently increased in acute hepatitis. This phenomenon has been thoroughly studied in 200 cases of hepatitis. The mean diameter was determined by the direct measurement of 100 cells. An important relation could be established between the mean diameter and the results simultaneously obtained from the bilirubin, galactose tolerance, Takata, Gros and prothrombin index determinations. There was no significant relation between the mean diameter and the corresponding values from the hippuric acid tests, the citric acid and the serum phosphatase determinations. The variations in the mean diameter and in the bilirubin concentration in serum ran parallel. In several cases one or more results of tests of hepatic function did not deviate significantly from the normal, while the mean diameter value simultaneously obtained was distinctly pathologic. Hence, the mean diameter determination may be of use in obtaining a reliable and complete statement of the condition of the hepatic parenchyma in cases of acute hepatitis. The standard deviation of the mean diameter (i.e., the anisocytosis) rose parallel with the mean diameter. There was no case of acute hepatitis, however, in which the standard deviation exceeded the limit of 0.86 micron.

Decreased Urinary Excretion of Rennin in Pernicious Anemia.—Sylvest explains why the secretion of gastric enzymes in the urine is decreased or ceases in patients with pernicious anemia. By means of a previously described method for the determination of the renninogen in the urine, the author examined 25 normal persons, 30 with pernicious anemia and 9 with another kind of gastric achlorhydria. The renninogen of the urine specimens was determined in relation to a known solution of pepsin (rennin) and stated in "rennin units" per 10 cc. of urine, 1 "rennin unit" being equal to 0.1 mg. of pepsin. The author concludes that in a patient who receives liver therapy for supposed pernicious anemia and gastric achlorhydria there are at present no methods to confirm or invalidate this diagnosis, unless the liver therapy is discontinued with the resulting inconveniences. Here a determination of the renninogen of the urine will furnish valuable information. Values above 0.3 "rennin unit" in 10 cc. of urine passed in the morning make it unlikely that the patient has this disease. That this observation is of more than theoretic value is proved by the fact that among a number of patients with pernicious anemia the author could exclude 2, in whom urorenninogen was normal. The fact that at the time of writing both persons were well without antianemic factor having been administered proves the error of the original diagnosis.

Klinische Wochenschrift, Heidelberg

27:449-488 (July 15) 1949. **Partial Index**

*Testing of Dibromodihydroxybenzil in Animal Experiments. G. Quadbeck—p. 449.
*Treatment of Wounds with Dibromodihydroxybenzil. R. Frey.—p. 452.
Amino-Thiouracils as Regulators of Metabolism. R. Kopf, A. Loeser and H. J. Bielig.—p. 455.
Changes in Histaminase Activity of Human Blood Produced by Various Vegetative Stimuli. W_4 Jacob and G. Stüttgen.—p. 457.

Dibromodihydroxybenzil in Animal Experiments.—Quadbeck tested the toxicity of 5,5'-dibromo-2,2'-dihydroxybenzil in rats. Dibromodihydroxybenzil in a solution of borate buffer proved to be relatively toxic when administered by parenteral route. Diacetyl-dibromo-dihydroxybenzil was well tolerated when administered by mouth. This compound is saponified to free dibromodihydroxybenzil in the intestine of the animals. The absorption ratio of the drug in the blood and in the urine was determined by quantitative colorimetry; 1 mg. of the drug was added to each 10 cc. sample of blood and the recovered amount of dibromodihydroxybenzil varied from 0.94 to 0.98 mg.

Treatment of Wounds with Dibromodihydroxybenzil.—Frey treated 100 patients, 11 with superficial ulcers, 6 with burns, frostbites and gangrene, 17 with suppurating wound cavities and abscess, 50 with recent accidental injuries or operative wounds, 13 with fistulas after gunshot fractures and osteomyelitis and 3 with chronic pyoderma or erysipelas, by local application of dibromodihydroxybenzil (5,5'-dibromo-2,2'-dihydroxybenzil) dusting powder or a 2 per cent dibromodihydroxybenzil solution in polyglycol ether. The longest duration of the treatment was forty-eight weeks. Dibromodihydroxybenzil is more stable than penicillin. In vitro it is effective in a more dilute solution than are the sulfonamide compounds, and it can be produced synthetically. It may be used as a wound disinfectant only by local application because it is inactivated in part by the serum. Its low solubility favors local application. Dibromodihydroxybenzil is less suitable for chemoprophylaxis of infection in recent wounds. In chronic wounds its value equaled or even surpassed that of the common wound disinfectants because of its slow absorption, bacteriostatic and curative effect. It proved superior to penicillin or sulfonamide compounds in hypersensitive patients or in cases of resistance of the pathogenic agents to those drugs. It proved to be particularly effective in extensive suppurating wounds, in refractory wound cavities and fistulas when applied as a solution, in wounds which have become resistant to other methods of treatment and in dermatomycoses. Combined or alternate treatment with other proved methods may be required.

Maandschrift voor Kindergeneeskunde, Leyden

17:67-98 (No. 3) 1949. **Partial Index**

Relapsing Bronchitis as Result of Carious Teeth? G. M. H. Veeneklaas and H. J. van Maanen.—p. 74.
*Streptomycin in Treatment of Tuberculous Meningitis. S. van Creveld and M. R. H. Stoppelman.—p. 77.

Streptomycin in Tuberculous Meningitis.—Van Creveld and Stoppelman say that, from March 1948 to May 1948, 7 children with tuberculous meningitis were treated at the Children's Clinic of the University of Amsterdam. The ages of the children varied between 15 months and 6 years. The children were treated with streptomycin in daily doses of 45 mg. per kilogram

of body weight, divided into six intramuscular injections. Three children were also given intraspinal injections of 100 mg. of streptomycin. Four of the 7 children died. Of the 3 surviving patients, 2 children aged 19 months and 6 years show severe mental defects. The only child who is now in good health was 15 months of age at the time of onset of the disease.

Medizinische Klinik, Munich

44:1041-1072 (Aug. 19) 1949. **Partial Index**

Clinical Observations on So-Called Serous Meningitis. H. Kalk and K. Nissen.—p. 1041.
Cytologic Method of Diagnosis of Cancer According to Papanicolaou. P. Stoll.—p. 1046.
Problems Connected with Surgical or Gynecologic Interventions During Pregnancy. W. Schaefer.—p. 1050.
Anamnesis of Stomach and Roentgenologic Observations; Comparison, with Special Consideration of Gastric and Duodenal Ulcers. H. Bonhag. —p. 1053.
*Twenty-Three Cases of Laboratory Infection with Q Fever. W. Kikuth and M. Bock.—p. 1046.

Laboratory Infection with Q Fever.—Kikuth and Bock report 23 cases of Q fever in 7 men and 16 women who were working with the same pathogenic strain in the authors' laboratory. It was a rickettsial strain which had been isolated by Herzberg from patients with atypical pneumonia, or Balkan grippe, and it had been given to the authors for further investigation. Not a single case of Q fever occurred among Herzberg's laboratory workers, but an epidemic resulted in the authors' laboratory after passages were made with the rickettsial strain which had been maintained in guinea pigs and mice. Inhalation of rickettsia-containing dust is probably the route of infection in man and in experimental animals. Not a single transmission of Q fever from man to man was observed among persons in contact with the patients, who were not isolated. Exhaustion, headache, fever, anorexia and the characteristic pulmonary symptoms of cough, blood-tinged sputum and light shadows in the lower lobes of the lungs on roentgenologic examination, were predominant in all the patients. The clinical diagnosis was established serologically in 17 patients. Treatment was symptomatic. All patients recovered. There were no recurrences.

Nordisk Medicin, Stockholm

42:1155-1184 (July 8) 1949. **Partial Index**

*Roentgenologic Differential Diagnosis Between Pulmonary Tuberculosis and Primary and Secondary Tumors Together with So-Called Radiation Fibrosis. S. Welin.—p. 1155.
When Does Tuberculosis Flare Up in Contralateral Lung After Collapse Therapy? P. Vaksvik.—p. 1158.
*Para-Aminosalicylic Acid and Streptomycin Therapy in Tuberculosis of Urinary Tract. Resorption, Renal Excretion and By-Effects of Preparation Together with Report on Cases Treated. G. Dahlström and H. Difs.—p. 1162.
Traumatic Angiopathy of Retina. P. Barfoed.—p. 1165.
Urethral Diverticuli in Women. A. Ingelman-Sundberg.—p. 1168.
Prolapse of Urethra in Women. R. Wilenius.—p. 1170.
Traumatic Rupture of Gallbladder. G. Eklöf.—p. 1172.
Hepatitis During Estrogen Treatment of Cancer of Prostate. O. Kløvstad. —p. 1173.

Roentgenologic Differential Diagnosis Between Tuberculosis and Tumor.—Welin states that distinction between pulmonary tuberculosis and primary and secondary tumor together with radiation fibrosis on the basis of clinical and roentgenologic observations may be difficult, especially in the case of tumors of the mucus and salivary glands, which, though often benign, have a comparatively grave pathophysiologic effect on the lung. Bronchial stenoses, solitary or multiple, are frequent in chronic pulmonary tuberculosis. Multiple stenoses are generally accompanied with inflammatory processes, while neoformations are to be expected with solitary stenosis, but this rule cannot be relied on. Two cases with inflammatory process and solitary bronchial stenosis and 1 case of tumor with multiple stenoses are reported. A pulmonary change of typical metastases-like appearance may occasion difficulty in diagnosis; an instance is described. The view expressed in the literature that the foci in miliary tuberculosis are larger in the upper parts of the lung than in the lower cannot always be upheld. In the usual preoperative and postoperative roentgen treatment of cancer of the breast changes often occur in the form of fibrous tissue; the history together with the location of the changes gives the diagnosis of radiation fibrosis. Roentgen diagnosis may be difficult especially in the early stages, when diagnosis should be made. The examinations must therefore be completed by bronchoscopy with biopsy; the result is usually decisive. Pulmonary tumors are accessible for biopsy in about 75 per cent of the cases; in the remainder they are too peripheral. There are cases in which definite etiologic diagnosis cannot be made with present day facilities.

Para-Aminosalicylic Acid and Streptomycin Therapy in Tuberculosis of Urinary Tract.—Dahlström and Difs report 5 cases of renal tuberculosis of ulcerocavernous type, in 3 of which para-aminosalicylic acid therapy resulted in decided improvement in the cystitis, considerable decrease in elimination of tubercle bacilli, decrease or disappearance of albuminuria, no change on the whole in sedimentation and no change in the result of urography and no aggravation in renal function during the treatment, which lasted from nine to twenty-two months. There were no noteworthy side effects. Similar results were attained in the fourth case with streptomycin therapy and twenty-six months of observation, and in the fifth, in which combined para-aminosalicylic acid and streptomycin therapy was used. On the basis of the results of treatment of chronic cavernous pulmonary tuberculosis, partly with para-aminosalicylic acid, partly with para-aminosalicylic acid and streptomycin in combination, and of experiments in animals the authors have now adopted combined para-aminosalicylic acid and streptomycin therapy in tuberculosis of the urinary tract. Prolonged para-aminosalicylic acid medication is given, preferably continued as long as there is bacteriuria, with not too brief series of streptomycin or dihydrostreptomycin treatment, and the usual hygienic-dietetic treatment. The daily dosage of 8 to 12 Gm. para-aminosalicylic acid is apportioned in four doses; whether larger dosage would be advantageous further experience will tell. The streptomycin dosage is 1 Gm. daily, in two to four injections; the optimal dose is not known. Sodium para-aminosalicylic acid seems to be resorbed and excreted more rapidly than para-aminosalicylic acid. No serious injuries have so far been observed on continued administration of para-aminosalicylic acid. The patients must be followed closely with regard to unspecific infections of the urinary tract, to be treated as usual, and close urologic observation is called for with reference to possible complications, especially the development of ureteral stricture and resulting hydronephrosis.

Semaine des Hôpitaux de Paris

25:2339-2388 (July 26) 1949. **Partial Index**

Congenital Malformations and Hereditary Malformations. M. Lamy. —p. 2339.
Congenital Syphilis in Young Infants. M. Lamy, M. L. Jammet, M. Aussannaire and J. Labesse.—p. 2344.
*Genetic Studies on Hypertrophic Stenosis of Pylorus. M. Lamy, C. Pognan, Marillier, J. Jammet and P. A. Cordier.—p. 2348.

Hypertrophic Stenosis of the Pylorus.—Lamy and co-workers report male twins with hypertrophic stenosis of the pylorus operated on at the age of 2½ months. A review of the literature showed that in 13 of 15 pairs of monozygotic twins both twins had pyloric stenosis and in the remaining 2 pairs only 1 of the twins presented this condition. Twenty-three pairs of dizygotic twins had been reported, and in 21 of the pairs only 1 twin had pyloric stenosis while in the remaining 2 pairs both twins presented this condition. Hypertrophic stenosis of the pylorus is a genotypic hereditary disease. Concordance is the rule and discordance the exception in monozygotic twins, while discordance is the rule and concordance the exception in dizygotic twins. Two hundred and twelve families with 556 children were studied. Two hundred and twenty-two children (179 boys and 43 girls) of the 556 had pyloric stenosis and 105 of the 222 were first born offspring. In 8 of the 212 families 2 children presented the condition, and in 1 family 3 children had pyloric stenosis. In 5 of the 212 families there were consanguineous marriages, about 2.36 per cent as compared with approximately 0.8 per cent of consanguineous marriages in the French population. A recessive monomeric autosome heredity seems highly probable. The percentage of persons with the defect, the incidence of familial cases and the larger number of consanguineous marriages in the ascendancy favor the recessive character of the condition. It is difficult to explain the predominance of the disease in the male sex. The predilection of the disease for the first born offspring has not been confirmed.

Book Notices

THE REVIEWS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES AND DO NOT REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED.

Pharmacology and Toxicology of Uranium Compounds with a Section on the Pharmacology and Toxicology of Fluorine and Hydrogen Fluoride. Edited by Carl Voegtlin, Ph.D., and Harold C. Hodge, Ph.D., Professor of Pharmacology and Toxicology, School of Medicine and Dentistry, University of Rochester, Rochester, N. Y. National Nuclear Energy Series, Manhattan Project Technical Section. Division VI. Volume I. [In Two Volumes.] Cloth. Price, $10. Pp. 1084, with illustrations. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 18; Aldwych House, Aldwych, London, W.C.2, 1949.

Until the present development of atomic energy, uranium and its compounds were of minor interest in medicine. Now, however, this element has assumed basic importance in all work connected with nuclear fission by chain reacting piles, and hence its pharmacology and toxicology have been under intensive study. The reports presented in the volumes herein reviewed should be important reference tools to medical workers in the atomic energy field.

The research reported in these volumes, conducted principally at the University of Rochester, is of a high order and was undertaken to solve a number of immediate problems which arose as by-products of the development of the atomic bomb. The introduction to these reports summarizes briefly but adequately the principal conclusions to be derived from the detailed discussions which follow. The chemistry of the uranium compounds is next discussed, since an appreciation of this subject is necessary in order to evaluate the biologic data presented in subsequent chapters.

One might question the amount of space devoted to a discussion of analytic methods, particularly in view of the fact that much of this material is repeated elsewhere in the book. Also, there seems to be little excuse for the chapter on statistical methods, which is exceedingly elementary and adds nothing to that which can be found in readily available texts on this subject. This chapter could have been omitted without interfering with the continuity of the remaining chapters.

The pathologic anatomy of uranium poisoning and the characteristics of uranium toxicity are exhaustively discussed; but, here again, some of this material is repeated several times in other sections of the two volumes. There follow next exceedingly detailed discussions, with tables, graphs and illustrations, of the toxicology of uranium administered by various routes, the major emphasis being placed on toxicity following inhalation. Although this may seem surprising, it must be remembered that one of the principal methods used for separation of uranium isotopes is by gaseous diffusion, thus making inhalation a likely route for poisoning. The distribution and excretion of uranium and the tolerance to uranium compounds receives detailed attention. Of fundamental importance are the discussions of the action of uranium on enzymes and proteins and the methods used for testing for uranium poisoning based on the knowledge of its action on enzymes.

The second volume ends with a short discussion of the toxicity following inhalation of fluorine and hydrogen fluoride.

The main criticism which can be leveled at these volumes is the lack of editing to eliminate unnecessary duplication, the inclusion of some irrelevant material and the lack of condensation of much of the data. Although it is usually a good idea to present all data available, oftentimes the point of a presentation may be lost in a maze of figures, charts and graphs. This appears to be true in the present instance. Although it was probably necessary, at the time these research projects were being conducted, to duplicate some of the studies, it seems hardly necessary to reproduce this duplication in the volumes reporting the results of the entire project. Despite these criticisms, these two volumes contain the most comprehensive and detailed information on the medical aspects of uranium and its compounds available today.

An Account of the Schools of Surgery, Royal College of Surgeons, Dublin, 1789-1948. By J. D. H. Widdess, M.A., L.R.C.P. & S.I., Librarian and Lecturer in Biology, R.C.S.I. Foreword by William Doolin, F.R.C.S.I., Hon. Librarian, Royal College of Surgeons in Ireland. Cloth. Price, $5. Pp. 107, with 16 illustrations. Williams & Wilkins Company, Mt. Royal & Guilford Aves., Baltimore 2, 1949.

The Royal College of Surgeons in Ireland here presents, under the able authorship of the librarian of the college, an authentic account of the origin and development of Irish surgical training institutions. It is the first separate work on this subject, containing a great deal of hitherto unpublished material and a great deal more that has been published from time to time but never collected.

"To write of this College and its Schools," remarks the author, "is to tell how surgery in Ireland freed itself from a medieval system of government which was devised for the regulation of various kinds of tradesmen." Among these tradesmen were the so-called barber-surgeons of that unenlightened day, who until the foundation of the college were represented by only one legally recognized authority, the Barber-Surgeons' Guild. From this unpromising beginning Mr. Widdess traces the difficult but unfaltering progress made to the present time, including many illuminating notes on the careers of such eminent figures as Sylvester O'Halloran, Samuel Croker-King and Abraham Colles.

The book is illustrated with portraits and fine architectural drawings. The style is conversational, and many quotable anecdotes and epigrams enrich it. This volume will make a unique contribution to the shelves of any library.

Skin Diseases in General Practice. By F. Ray Bettley, T.D., M.D., F.R.C.P., Physician for Diseases of the Skin, Middlesex Hospital, London. Cloth. Price, 21s. Pp. 260, with 96 illustrations. Published on behalf of The Practitioner, 5 Bentinck St., London, W.1, by Eyre & Spottiswoode, Ltd., 14-16 Bedford St., Strand, London, W.C.2, 1949.

This small textbook has for its theme the commonly recognized fact that the large majority of dermatologic cases fall into ten or a dozen common categories. Recognizing this, the author has limited his discussion to the commoner disorders, since it would be impossible to include any of the less common conditions in a short treatise. The subjects covered are: eczema in its varied phases, occupational dermatoses, seborrheic dermatitis, acne, psoriasis, impetigo contagiosa, common fungus infections, rosacea, perineal pruritus, alopecia areata, parasitic diseases, nevi and epithelial tumors.

The clinical features of each of the disorders is covered in a comprehensive fashion. The sections on therapy are based largely on the author's personal experiences and are given in much more detail than is the case in the usual large textbooks on dermatology. Not only are the agents to be used discussed, but details in the methods of use are covered thoroughly.

Issue might be taken with some of the author's ideas, notably as to the usefulness of desensitization methods of both general and local type in the treatment of eczema, since these are hardly measures which could be handled adequately by any except those with special experience.

A valuable addition to the book is a comprehensive list of the substances to be used in patch testing together with the proper dilution and the vehicles to be employed. For the diseases which are covered in this volume, the practitioner will find the book a useful addition to his library.

Autobiography of Dr. Robert Meyer (1864-1947): A Short Abstract of a Long Life. With a Memoir of Dr. Meyer by Emil Novak, M.D. Cloth. Price, $2.50. Pp. 126, with 1 portrait. Henry Schuman, Inc., Publishers, 20 E. 70th St., New York 21, 1949.

Meyer's autobiography, a notable addition to medical autobiography, appeared first in the "History of Medicine and Allied Sciences" under the title "A Short Abstract of a Long Life." In this book are also an interesting memoir of Meyer by Emil Novak in Baltimore, a complete list of Meyer's writings, arranged according to the years of publication, his histogenetic classification of ovarian tumors and a good subject index. The scientific eminence which he achieved will assure him "a permanent and prominent place in the history of embryology, pathology, gynecology and obstetrics."

Lehrbook der Stimm- und Sprachheilkunde. Von Dozent Dr. Med. R. Luchsinger, leitender Arzt der Abteilung für Sprach- u. Stimmkranke der oto-, rhino-, laryngologischen Klinik und Poliklinik in Zürich, und Dozent Dr. Med. G. E. Arnold. Paper. Price, $14.40. Pp. 431, with 163 illustrations. Springer-Verlag, Mölkerbastei 5, Vienna 1, 1949.

The publication of this informative book was considered necessary by the authors because no similar work had been compiled in Austria, Germany and Switzerland for the past ten years. As stated in the preface, Drs. Luchsinger and Arnold analyzed the latest results of experimental investigations in the field of voice and speech. Due emphasis was also given to the importance of psychologic problems. The book is divided into two parts. In the first part, Luchsinger deals with the normal and pathologic functions of the voice. In the second chapter, he gives in detail a review of vocal acoustics, the study of vocal cord movements, electroacoustic voice analysis, laryngostroboscopy, Roentgen examination of the larynx during its various functions and laryngoscopic measurement of laryngeal dimensions. The third chapter gives the physiology of the laryngeal musculature, the development of voice and an analysis of its function. Many studies pertaining to hereditary factors influencing voice quality are reviewed.

Equally detailed is the presentation of voice pathology. The first chapter on vocal cord nodes leads up to congenital asymmetries associated with voice disorders. It also deals with vocal symptoms resulting from endocrine disturbances. Chapter V is concerned with paralytic conditions of both laryngeal nerves and the sternothyroid muscle, which has been recognized to be important for normal voice production. Traumatic dysphonias and the voice of persons who have undergone the laryngectomy are considered in the next chapter. Dr. Luchsinger divides functional voice disorders into four main groups: voice fatigue of singers and speakers (phonasthenia), vasomotor monochorditis, incorrect vocal habits (habitual dysphonias) and psychogenic dysphonias. The two latter forms are subdivided into hyperkinetic and hypokinetic types.

In the second part of the book, G. E. Arnold begins with a detailed description of speech physiology. His chapter on hereditary speech biology is partly based on Luchsinger's previous publications. A chapter on the manifold connections between constitution and speech leads to a concise abstract of speech psychology from the pen of the Viennese professor, Dr. F. Kainz. The chronologic analysis of infantile speech development and methods of clinical examinations conclude this general section. This section also contains an article on psychologic examinations of children by Dr. E. Baar (Vienna).

In a special section that follows, Arnold deals with the various forms of central speech delay. In this category belong delayed speech development, hearing-mutism, congenital auditory imperception, functional dyslalia, agrammatism and reading disability. Otogenic dyslalias resulting from congenital or acquired deafness and the mechanical dyslalias connected with malformations, injuries or paralytic conditions of the peripheral speech organs are presented in chapters IX and X. Also included are the different forms of nasal speech (rhinolalia) and the problems of cleft palate speech. Another chapter is devoted to speech disorders due to mental retardation, aphasias and dysarthrias. The latter are presented in a new classification on the basis of symptoms as well as causes. The chapter on stuttering (dysphemia) is worthy of special interest; with impartial objectivity the often opposed theories of a great number of authorities both in this country and in Europe are reviewed. Cluttering, voluntary silence, several forms of purely psychogenic speech disorders and some other types of neurotic disturbances are also discussed.

The book is clearly written and well documented. Although some of the illustrations in the first part are not typographically clear because of technical difficulties in postwar Europe, they are illuminating as a whole. Each chapter is followed by an unusually extensive bibliography comprising the pertinent new literature of the whole world. Together with a carefully prepared index of names and subjects, it makes the work convenient for reference and study. Orientation is also facilitated by the systematic subdivision of each pathologic unit into definition, classification, etiology, pathology, symptomatology, diagnosis, therapy and prognosis.

Hospital Personnel Administration. Section I: The Development of Sound Personnel Practices in Hospitals. M3-48. Section II: Conference Techniques. M6-49. Paper. Price, $1.50; $2.25. Various pagination; Pp. 141. Committee on Personnel Relations, Council on Administrative Practice of the American Hospital Association, 18 E. Division St., Chicago 10, 1948; 1949.

Section I.—The Committee of the American Hospital Association, which prepared this booklet, has performed a great service. It should not only make the task of the hospital administrator easier but also result in greater contentment and increased harmony between the medical and nonmedical hospital personnel.

This is not intended as a guide book of hard and fast rules. It does, however, contain general discussions which should be adaptable to many kinds of institutions. Formulation of policy regarding personnel is thoroughly discussed. Other weighty problems, such as selection and training of supervisors, employee rating and promotion and employee participation, are discussed sensibly and carefully. Every hospital superintendent and everyone having to do with hospital personnel administration would profit by giving this booklet careful study.

Section II.—This booklet deals with methods of conducting conferences of hospital personnel, how to select the leaders of such conferences and the problems encountered in running them. Although it was devised primarily for conferences among hospital administrators and their staffs, those who conduct committee meetings in other fields could benefit by many of the suggestions contained herein.

You and Your Fears. By Peter J. Steincrohn, M.D., F.A.C.P. Introduction by C. Charles Burlingame, M.D., F.A.C.P. Cloth. Price, $2.50. Pp. 224. Doubleday & Company, Inc., Garden City, N. Y.; 14 W. 49th St., New York 20, 1949.

In this volume Dr. Steincrohn, who has written seven other books for the laity, discusses fear and its effects on health. The author writes as an internist and not as one trained in psychiatry, and therefore he makes no pretense at considering the deeper psychopathology of the conditions under discussion. His thesis is based on his belief "that it is time the emotional problems of human beings were set down as viewed by the internist and general practitioner. For it is by such physicians that these patients are first seen. In fact, hundreds of thousands never get to the psychiatrist at all" (page 22).

The chapters all have popular headings, for example, "Is Your Doctor a Curious Cuss?" and "Personality is Like a Violin." In chapter 20 he warns against too much exercise and finds that too many Americans are "exercise mad." In chapter 28 he outlines his ideas on medical care.

The book is a pleasant, exhortative type of work, and it is probable that the author uses the so-called common sense approach and is authoritarian or philosophic in his attack on the problems he encounters, depending on the indications. In books of this kind there is always a danger that the problem will seem to be oversimplified, but this fault is not too apparent in this volume. In fact, practitioners could read the work with some profit.

Atlas of Roentgenographic Positions. By Vinita Merrill. In Two Volumes. Cloth. Price, $30. Pp. 294; 295-663, with illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1949.

This beautifully printed and profusely illustrated two volume work covers a wider field than its title indicates and should prove to be extremely popular with x-ray technicians, for whom it is intended. Its cost is so great, however, that sales probably will be restricted chiefly to institutions.

All important positions seem to have been included, and such faults as occur in the other material are chargeable to the present status of radiologic thinking rather than to the author, whose self-appointed task has been reporting rather than revising or influencing thinking. It is not true that the voltage of the x-ray beam must be adjusted critically to the thickness and density of the part being examined or that the Potter grid should not be used for sinuses or that visual control of development of films is essential in the examination of certain parts of the body; but until these and similar superstitions are abandoned by radiologists, such compilers as Miss Merrill must be excused for incorporating them in books like this one.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

CRAMPS IN HANDS AND LEGS

To the Editor:—I have many patients who have cramps in the hands, legs and feet, and I would like to know whether the cause is really known.

Wm. V. Vander Voort, M.D., Battle Creek, Mich.

To the Editor:—We have had a number of cases in which the patient complains of severe cramping of the legs, which seems to come on more frequently at night, especially present in the gastrocnemius muscles. In 1 patient the cramping began approximately five years ago. She gives a history of endometriosis with surgical treatment in 1946. Recently the cramping has become more frequent, lasting for thirty minutes to an hour. The shelving edge of the gastrocnemius muscle of the right leg has atrophied during the past year and is gradually becoming more pronounced. We would appreciate advice on the cause and treatment.

J. M. Hesser, M.D., Benson, Ariz.

ANSWER.—The actual cause of, or mechanism producing, muscular cramps is not known. However, certain factors affecting the body metabolism are frequently associated with painful or painless cramps. Sodium chloride balance is one of them. Cramps occur when the intake of sodium chloride is too low or the output is too high. In cholera, for example, loss of sodium chloride occurs as the result of the diarrhea and prolonged muscular pain, severe in character, may be a prominent symptom. A similar mechanism is seen in miner's cramps, owing to the loss of sodium chloride in sweat. Pain in both cholera and miner's disease may be relieved by the addition of salt to the diet.

Painless cramps occur after exercise, even after such minor muscular movements as knitting or writing. Only the small muscles are usually involved. A few moments of rest and massage are almost always sufficient to overcome the muscular spasms. It is only when the larger muscles are involved, such as those in the legs, back and abdomen, that painful cramps result. Although a disturbance of sodium balance gives rise to cramps, Hall (Hall, A. J.: Cramp and Salt Balance in Ordinary Life, *Lancet* **2**: 231 [Aug. 16] 1947) believes that the large majority of those who suffer from cramps in ordinary life are not in abnormal balance. A salt-free diet may result in cramps, usually painless, a factor which should be kept in mind in treating patients with cardiovascular disease.

To insure an ample intake of sodium chloride is the first step in treating patients complaining of cramps in ordinary life. Second comes avoidance of muscular fatigue, particularly in muscles already affected by myopathic degeneration such as that seen in dystrophies, atrophies or subsequent to trauma. Extreme ranges of heat or cold are well known causes of cramps. The swimmer's cramp in cold water and the mountain climber's cramp, due to fatigue and cold, are well recognized examples.

Cramps are a symptom of poisoning, associated with avitaminosis. The favorable response to vitamin B_2, lactoflavin and riboflavin in ameliorating the muscular pains associated with chronic carbon monoxide poisoning has been demonstrated.

Cramps are associated with a lowered blood calcium level and are seen in rickets and pregnancy because of this condition. Alkalosis of any type may cause cramps, but the mechanism of the muscular disturbances due to an increase in blood p_H is not understood.

CONGENITALLY SMALL PENIS

To the Editor:—Please discuss any recent treatment that relates to a 37 year old married man with a small penis, similar to that of a 10 year old child. Prostatic findings are negative, and testes are normal. Would injections of testosterone propionate or gonadotropic hormone be helpful in stimulating normal development? Would circumcision be a remedy?

M.D., Indiana.

ANSWER.—The patient has a congenitally small penis, and testosterone propionate and chorionic gonadotropin will probably not be effective in increasing its size. These materials are valuable in increasing the size of the penis only when there is a definite testicular deficiency. As the testes of this man seem normal, they probably have produced enough hormone to stimulate the development of his penis to its maximum. In all hormone therapy, it is necessary to consider not only the effectiveness of the stimulating agent but also the ability of the organ concerned to respond to stimulation. In this instance, the ability of the penis to respond to stimulation seems definitely limited.

URINARY RETENTION IN SPINA BIFIDA

To the Editor:—What is the most effective management of the urinary tract of a 4 year old child with congenital spina bifida associated with an atonic bladder and urinary overflow incontinence? She has had at least one episode of acute pyelonephritis. Treatment with sulfonamide drugs appears successfully to combat the acute infections. However, the fundamental problem of urinary stasis and potential infection continues to exist. Would small maintenance doses of a sulfonamide drug be advisable prophylactically? Would an indwelling catheter be advisable? Would such parasympathomimetic agents as furfuryl trimethyl ammonium iodide and carbachol be recommended to promote bladder emptying, or would the undesirable side effects offset their value? The residual urine is at least 150 cc. The bladder edge is frequently palpable at the umbilicus. Operation is to be performed when the child is older. Please outline a detailed program of management of the urinary tract. M.D., California.

ANSWER.—Retention of urine with varying degrees of incontinence is a frequent complication of congenital spina bifida. Retention in these cases is usually caused by some form of obstructive uropathic condition of the vesical neck. The types of obstruction usually found in cystoscopic examination are: contraction of the vesical neck, bars and hyperplasia of the urinary sphincter. In some cases the vesical neck may appear to be normal, but spasticity or contraction is present. Fortunately, a method is available to remove the cause of urinary retention, namely, by means of transurethral resection of the obstructing tissue.

The child in question is not too young for this operation, and it should be performed without further delay. The incontinence may be due to overflow, but frequently in these cases it is caused by an incompetent external urethral sphincter. In some cases the incontinence is corrected by removal of the obstruction at the bladder neck, and in others it is necessary to perform a plastic operation on the external sphincter. This can be done, preferably, in later years. The incontinence may be so greatly improved after resection that it is no longer of serious importance. If the retention is of great degree or has existed a long time, extensive renal damage may result. It would be well to determine the renal function before attempting resection. Chronic urinary infection is a common complication in this condition, and there are frequent episodes of acute infection; as you stated, they will continue in spite of medication as long as urinary stasis exists. The infection usually disappears with the correction of urinary retention.

RHEUMATIC DISORDERS OF THE LOW BACK

To the Editor:—A patient has had for years arthritis of the lumbosacral part of the spine and/or sacroiliac joints. The patient had been bedridden for three days when first seen. Adhesive strapping of the lower part of the back by another physician had not helped him. At that time at the points of maximum tenderness in the lumbosacral region I injected 2 per cent procaine—without epinephrine—about 15 cc., and did a block of the left sciatic nerve. The patient was much improved and slept for several hours, which he had been unable to do for the previous two nights. He is now able to come to my office; the pain in the spine is gone but some pain is still present in the upper medial quadrant of the left buttock. Another procaine block was done, with 10 cc. of the 2 per cent solution. Is procaine injection an accepted treatment for this condition? What else could have been done? What follow-up treatment is indicated?

John F. Noguera, M.D., Kingsville, Md.

ANSWER.—Proper treatment of rheumatic disorders of the lower part of the back differs, depending primarily on the nature of the disease. Differential diagnosis is the first requisite. Too little information is given in this case to allow proper diagnosis; therefore exact treatment cannot be offered.

Complete history, physical examination and laboratory data, including roentgenograms, will in the majority of cases allow definite and correct diagnosis. Many persons with low back pain and stiffness do not have arthritis but suffer from postural strain, intervertebral disk syndrome, fibrositis or other nonarticular disorder. Arthritis of the spine, except in rare instances, is one of two types—rheumatoid spondylitis or osteoarthritis (degenerative disease of the joints). For each type of spinal arthritis a program of treatment including a firm bed, added rest, regular analgesia (salicylic acid derivatives usually suffice, narcotics may be needed for a short while), heat applied to the back (baths, warm packs, infra-red lamp), therapeutic exercises and sometimes antispasmodics is usually beneficial. Other treatment differs, according to the type of disease. For rheumatoid spondylitis roentgen therapy may be helpful. Osteoarthritis of the spine is often relieved by reduction of weight to normal, spine traction and an orthopedic back support. Persistence in treatment is generally required over many weeks or months.

Nonarticular back syndromes are often relieved by the aforementioned general measures as treatment for spinal arthritis. In addition, massage may be helpful for fibrositis; if herniated fat accounts for recurrent or persistent back pain, isolation and excision of the offending tissue may be required for lasting

relief. Surgical removal of the protruding intervertebral disk is required in some cases.

In any painful disorder of the back, injection of the site of tenderness and pain or the root of nerves supplying the painful tissue may be relieving sometimes for a few hours only, sometimes for longer periods; in most instances this treatment alone will not suffice, for it does not correct the underlying disease or give sustained analgesia. It is always wise to identify the cause of the pain and, if possible, correct or control the disease process. That relief followed sciatic nerve block in the patient described strongly suggests the existence of an intervertebral disk lesion, for this is the commonest cause of sciatica with or without back pain. Studies to clarify the nature of the pathologic change are strongly recommended in this case; details of treatment then can be more confidently planned.

PROLONGED ACTION OF PENICILLIN

To the Editor:—**Is the prolonged action of so-called ninety-six hour penicillin G procaine salt in aluminum monostearate gel due to delayed absorption or delayed excretion, or both? If due to delayed absorption, what is the average effective blood level on the first four days after injection of 300,000 units intragluteally, and how does that compare with the older type of penicillin G sodium in oil?**

R. W. Mueller, M.D., Los Angeles.

ANSWER.—Prolonged duration of assayable serum penicillin concentrations following injection of suspensions of procaine penicillin in oil with 2 per cent aluminum monostearate is due to delayed absorption from the site of administration. This is due to the physical properties of the gel produced by addition of aluminum monostearate. Average serum penicillin concentrations, in units per cubic centimeter, following administration of 300,000 units of the preparation, as referred to in the question, obtained in one laboratory were as follows:

Hours After Injection	Sodium Penicillin G in Peanut Oil with 4.8 per Cent Wax	Procaine Penicillin G in Sesame Oil with 2 per Cent Aluminum Monostearate
4	0.6	0.25
12	0.08	0.10
24	0.02	0.08
48	0.00	0.06
72	....	0.04
96	....	0.04

The third part of this question could be answered only with respect to a given situation, since effective blood level is determined by both specific pathologic state as well as bacterial sensitivity.

IODOFORM

To the Editor:—**Can the small amount of iodoform contained in several proprietary preparations advocated for the treatment of respiratory afflictions produce toxic reactions? These preparations contain about 10 or 20 mg. of iodoform, together with camphor, menthol and other substances, in a vehicle of peanut or other oils and are given by intramuscular injection. Among these are camirol® and gobromol®. Could this amount of iodoform theoretically produce toxic symptoms such as those described in Sollmann's textbook (Sollmann, T.: A Manual of Pharmacology and its Application to Therapeutics and Toxicology, Philadelphia, W. B. Saunders Company, 1948)? If so, is there any way of proving that symptoms were due to this substance?**

M.D., California.

ANSWER.—Little information is available concerning the toxicity of iodoform-containing preparations such as camirol® and gobromol.® Neither preparation has been accepted by the Council on Pharmacy and Chemistry, and their value in the treatment of diseases of the respiratory tract is questionable.

Most cases of iodoform poisoning have occurred after its prolonged use on wounds and in surgical dressings. Its propensity for producing acute poisoning varies among different persons; however, except under conditions of extreme susceptibility or frequent and prolonged use, it is doubtful whether toxic reactions could be ascribed to the iodoform content of these preparations. Camphor is slowly and inconsistently absorbed from oil solutions, and its presence intramuscularly may produce serious local inflammatory changes. Menthol, in the concentrations present, is not considered to have any deleterious effects.

There is no conclusive method to prove that untoward effects in a susceptible person were due to the iodoform content of these preparations. A comparatively high blood iodine level would lead one to suspect this substance; however, the absence of such would not exclude iodoform as a possible cause of adverse reactions.

BANCROFTIAN FILARIASIS

To the Editor:—**A 32 year old man has migratory myalgia with swelling of the involved muscles; this usually is in muscles of the forearm, arm, shoulders and legs, both extensor and flexor groups. The symptoms came on shortly after the patient was discharged from the service after having spent some time in the South Pacific. Physical examination did not reveal abnormalities other than infected tonsils and tenderness of the muscle groups when they are swollen. Laboratory examination reveals a normal sedimentation rate and total blood cell count but with usually 30 to 40 per cent eosinophils. The last smear did not show an abnormal eosinophil count. The result of a skin test for Trichinella was negative. Biopsy of gastrocnemius muscle did not reveal Trichinella. The electrocardiogram was normal. The man obtained temporary relief with quinacrine hydrochloride and also with the use of tripelennamine hydrochloride. Sodium salicylates gave no relief. There is no history of malaria. Are there obscure tropical diseases with this picture? Could this be an allergic response? The symptoms have been present now for over two years.**

M.D., Michigan.

ANSWER.—The symptoms in this case are typical of the allergic manifestations of bancroftian filariasis, but it may be impossible to confirm the diagnosis. Spontaneous cure is likely within another year. Treatment with antimonials might be of service.

OSTEOARTHRITIS

To the Editor:—**Is there any new treatment for chronic degenerative osteoarthritis? I have a patient in the hospital with beginning ankylosis of both elbows, wrists and knees. She does not have fever.**

R. E. Mitchell, M.D., Fort Stanton, N. Mex.

ANSWER.—There has not been any recent advance in the treatment of osteoarthritis. Measures which continue to prove helpful include rest and support of the involved joints, active exercises to maintain and improve joint and muscle function and the application of heat. The wrists may be supported in extension with light plaster or aluminum splints, and the knees should benefit by limiting the amount of weight bearing and by advocating the use of crutches. Primary involvement of the elbows and wrists with ankylosis is encountered rarely in osteoarthritis. A more likely diagnosis in this instance is rheumatoid arthritis, possibly with secondary osteoarthritic changes in the knees. The diagnosis in this patient should be reviewed. An increased sedimentation rate, inflammatory changes of soft tissue and roentgenologic evidence of loss of bony substance favor a diagnosis of rheumatoid arthritis.

REMOVAL OF UTERUS

To the Editor:—**Is there any logical proof for the belief that removal of the uterus produces symptoms of the climacteric or contributes to the production of symptoms of the climacteric other than from a psychiatric basis? Is there any evidence of primary endocrine function of the uterus? Does removal of the uterus produce atrophy of the ovaries or discontinue the cycle of follicle-corpus luteum development in the remaining ovary or ovaries?**

Donald L. Meamber, M.D., Yreka, Calif.

ANSWER.—There is no evidence that the uterus produces a hormone. However, the female genital apparatus should be thought of as a unit, and the integrity of any part of it appears to bear some relationship to the integrity of the whole. There is some evidence to suggest that the ovarian function of women who have had hysterectomies is not as satisfactory as that of women who have an intact uterus. However, the data are unsatisfactory, and a detailed study of this problem would be worth while.

COPPER COLORED ERUPTIONS

To the Editor:—**A patient who has been treated for syphilis has the copper-colored eruptions on the arms and legs. What will remove this discoloration?**

J. F. McKee, M.D., Johnston City, Ill.

ANSWER.—Ordinarily, pigmented lesions of early stage syphilis disappear with time. They fade more quickly after adequate antisyphilitic treatment. Occasionally, however, the pigmented spots persist despite such treatment; but these, too, clear up with time. Unfortunately, there is no treatment to hasten the process.

POSTMORTEM ROENTGENOGRAM OF BONES

To the Editor:—**Are roentgenograms of bones taken post mortem as likely to show pathologic processes as those of living persons?**

Anthony M. Susinno, M.D., Palisades Park, N. J.

ANSWER.—Yes; post mortem there should be no significant difference in appearance of the bones, but after mutilation of soft tissues some bizarre additional patterns may be added because of air and soft tissue density contrasts.

CONDYLOMATA ACUMINATA

To the Editor:—A French girl aged 25, married, in good health and two months' pregnant, complains of burning on urination and progressively increasing difficulty and pain in coitus. Examination revealed the entire vagina, its walls, fornices, the vaginal portion of the cervix uteri, labia, urethral meatus, and mons pubis and perineum to be studded with multiple warty excrescences. The warts were filiform, sessile, moist and dry, of variable size and configuration, being from pinhead to bean sized. There was also a profuse vaginal discharge. The warts and skin were macerated, and there was an unpleasant odor. Vaginal examination was uncomfortable to the patient. Cervical infection appeared minimal. Smears of vaginal secretions, the cervix and the urethra did not reveal gram-negative intracellular or extracellular diplococci which resembled gonococci; repeated dark field examinations of the secretions failed to reveal Treponema pallidum. The result of a standard serologic test of the blood for syphilis was negative. The woman stated that this was her first pregnancy. She denied having had any symptoms of syphilis or gonorrhea. Trichomonads were not demonstrated. The patient denied having taken a douche, having used any medicine or having had coitus with anyone other than her husband. The latter did not present evidence of similar lesions on his hands or genitalia and denied ever having had such lesions. Regional adenopathy was not present. The urinalysis revealed an abnormally large number of epithelial and white blood cells, although abnormal organisms were not noted. Biopsies were not done. Do these represent "warts of pregnancy" per se, with the likelihood of their disappearance after termination of gestation, or are they venereal (viral) in origin? Do they seem to be related to those supposedly described by Bricker in 1900?

Robert H. Maschmeyer, M.D., Shoals, Ind.

ANSWER.—Unfortunately some physicians believe that all warts on the vulva and in the vagina are venereal in origin. This is not true. Warts are due to viruses. The warts described in this patient are moist warts, generally known as condylomata acuminata or venereal warts. An irritating discharge, such as occurs in gonorrhea and also local hyperemia, predisposes to the development of warts on the external genitals, but the actual cause is a virus. The lesions vary in appearance, depending on the conditions at the site of inoculation.

Because of the friction of the labia, warts in this area usually become macerated and spread to nearby structures as the direct result of contact. Hence all parts of the genitals which contain warts must be kept clean with mild antiseptics. The warts disappear spontaneously during pregnancy in some cases but usually after delivery. If a vaginal discharge is present it must be treated. The warts may be scraped off with a scalpel and the bleeding stopped with caustics such as silver nitrate or carbolic acid. Perhaps the best treatment at present is the use of podophyllum resin. A 25 per cent podophyllum ointment is applied with an orange stick or similar device to every portion of the condyloma, including the surface and all crevices. Because podophyllum is highly irritating, the surrounding normal skin must be covered with a mild anesthetic ointment or Lassar's paste. To avoid spreading of the podophyllum ointment when the patient gets up to walk, she should be kept in the lithotomy position for at least twenty minutes. There is no immediate reaction, but pain usually ensues in six or eight hours. The medicament should be washed off three to six hours later with bland soap and water, preferably by the patient's getting into a bathtub. A mild anesthetic ointment may then be applied over the lesions. During the next twelve hours there is a pronounced local inflammatory and edematous reaction. On the second to the fifth day the lesions usually shrivel and drop off. In some instances there is no pain from the treatment.

TAY-SACHS DISEASE

To the Editor:—A family had 1 male child, who went through the usual stages and died at the age of 14 months. Seven months ago, about ten years after the first pregnancy, the wife gave birth to a female baby, who appeared normal until recently. The baby is alert and recognizes its parents and other persons. However, she is unable to sit up, turn over or reach for things. The pediatrician and the eye consultant have found the red spot in the macula typical of hereditary mongolian idiocy, or Tay-Sachs disease. Is there anything that can be done for children with this condition?

Louis H. Merker, M.D., Bronx, N. Y.

ANSWER.—The condition described is consistent with the diagnosis of Tay-Sachs disease. It is hardly accurate to use the term "hereditary mongolian idiocy." Mongolism is altogether different in its clinical manifestations and over-all problems and presumably of different causation.

Tay-Sachs disease is a progressive familial disease with involvement of the brain, retina and spinal cord. The history of the "male child that went through the usual stages" lends much weight to this diagnosis, the cause of which is not known. Vitamin therapy would be an experimental rather than a rational procedure. Whatever the process is and whatever the significance of the lipid infiltrations of the retina may be, there is no reason to suppose that they represent an infectious process which would respond to chemotherapeutic agents. Prognosis is unfavorable, with life expectancy ordinarily about two years.

RESPIRATORY INFECTION

To the Editor:—A patient has been ill for about three years with a respiratory infection, the cause of which has been identified as yeastlike organisms, belonging to the Saccharomyces group. Any information you have on this subject would be greatly appreciated.

Ara D. Sharp, M.D., Albion, Mich.

ANSWER.—Probably the yeastlike organisms of the Saccharomyces group (either Torula or Monilia in the new classification) are merely present as saprophytes. Monilia are found in the oropharynx of a large proportion of normal persons and are often present in large numbers in chronic pulmonary diseases like bronchiectasis, abscess, neoplasm and tuberculosis. It would be of primary importance in the case described to determine whether any underlying pulmonary disease exists. If so, treatment should be directed at the primary disease. No satisfactory specific treatment has been devised against yeast or yeastlike micro-organisms in the respiratory tract. Iodides, vaccines, antibiotics and chemotherapy are of no value.

STERILIZATION OF RUBBER GOODS

To the Editor:—What is the best way to sterilize rubber goods, such as rubber balloons, catheters and enema tubes, outside of boiling or autoclaving. Can you suggest some chemical solution which will not deteriorate the rubber.

Otis F. Lamson, M.D., Seattle.

ANSWER.—Rubber goods to be used in surgical operations should be autoclaved or boiled. Chemical sterilization is usually not adequate. Autoclaving for ten minutes at 252 F. will usually suffice, and this is more dependable than boiling. Rubber goods, such as gastric suction tubes, should be thoroughly washed with soap and water after use, and then soaked in 70 per cent alcohol overnight. Bichloride of mercury solutions can also be used, but are perhaps inferior to alcohol. Solutions of "lysol" and benzalkonium chloride make rubber sticky, and so are not usually satisfactory. A chemical cleansing method such as this is adequate for rubber goods which are not to be used at the operating table.

HEAD INJURIES

To the Editor:—In all cases of head injury, particularly in children, laymen invariably try to keep the patient awake. Is there any rationale which justifies this popular belief?

Water Newman, M.D., Springfield, Mass.

ANSWER.—In head injuries, efforts to keep the patient awake, by talking to him, shaking him, moving him or making him walk, will do harm. Such patients should be spared all effort that would increase the amount of damage through the cardiovascular effects of exertion. Management should be under the direction of a good surgeon—preferably an experienced neurosurgeon. Apparently the basis for belief that patients with head injuries should be kept awake is the fact that this procedure is often followed to combat the effects of narcotic drugs.

REPEATED USE OF SAME BLOOD DONOR

To the Editor:—Is there any reason why a person should not receive repeated blood transfusions from the same donor?

M.D., Bolivia.

ANSWER.—Repeated blood transfusions from the same donor may result in sensitization to factors peculiar to the donor's red cells. Therefore, compatibility tests are essential before each transfusion is given. When unusual sensitization is suspected, compatibility tests should be done with a protein medium as well as with isotonic sodium chloride solution.

DANGER OF RADIATION EXPOSURE

To the Editor:—In "Queries and Minor Notes" (August 13, p. 1249) part of the answer to the first question on "the danger of radiation exposure" is misleading. I refer particularly to the third paragraph, which should have been amplified as follows:

The fact is that danger to the fetus in utero from exposure to roentgen rays may arise when part of the abdomen corresponding to the pregnant uterus is directly exposed to a large dose of rays. Then the effect may take one of two forms or both of them. The growth of the fetal skull, and secondarily of the brain, may be retarded or arrested, and the fetus may die or miscarriage may result. When other parts of the mother's body are exposed to the rays, the fetus is not likely to be affected unless radiation treatment is sufficiently intense to cause severe radiation sickness. Sterility in either sex can arise only from direct exposure of the gonads, either to a single large dose or to repeated small doses. Sterility cannot occur from exposure of other parts of the body.

A. U. Desjardins, M.D., Rochester, Minn.